Integrative analysis of type-I and type-II aberrations underscores the genetic heterogeneity of pediatric acute myeloid leukemia

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Design and Methods

DNA and RNA isolation

After thawing the available appropriately frozen bone marrow or peripheral blood samples, leukemic cells were isolated and enriched as previously described.[1] Morphological confirmation of blast percentages was confirmed on cytospins stained with May-Grünwald-Giemsa (Merck, Darmstadt, Germany). Leukemic cells were lysed in TRIzol reagent (Gibco BRL, Life Technologies, Breda, The Netherlands). Genomic DNA and total cellular RNA were isolated according to the manufacturer's protocol with minor modifications.[2]

Cytogenetic analysis

Leukemic samples were routinely investigated for cytogenetic aberrations by G-, Q-, or R-banded karyotyping, and were screened for recurrent non-random genetic aberration characteristics for AML, including *MLL*-rearrangements, inv(16)(p13q22)/ t(16;16)(p13;q22), t(8;21)(q22;q22) and t(15;17)(q22;q21), using either RT-PCR and/or fluorescent *in situ* hybridization (FISH). These analyses were carried out by each study group. When material was available but data were missing, screening for these aberrations was carried out by the Laboratory of Pediatric Oncology/Hematology at Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands. In addition, patients under the age of 18 months were screened for the presence of t(7;12)(q36;p13) by FISH. The probes used were five cosmid clones covering the breakpoints in the ETV6 gene and a PAC clone (RP5-1121A15) containing the *HLXB9* gene.[3]

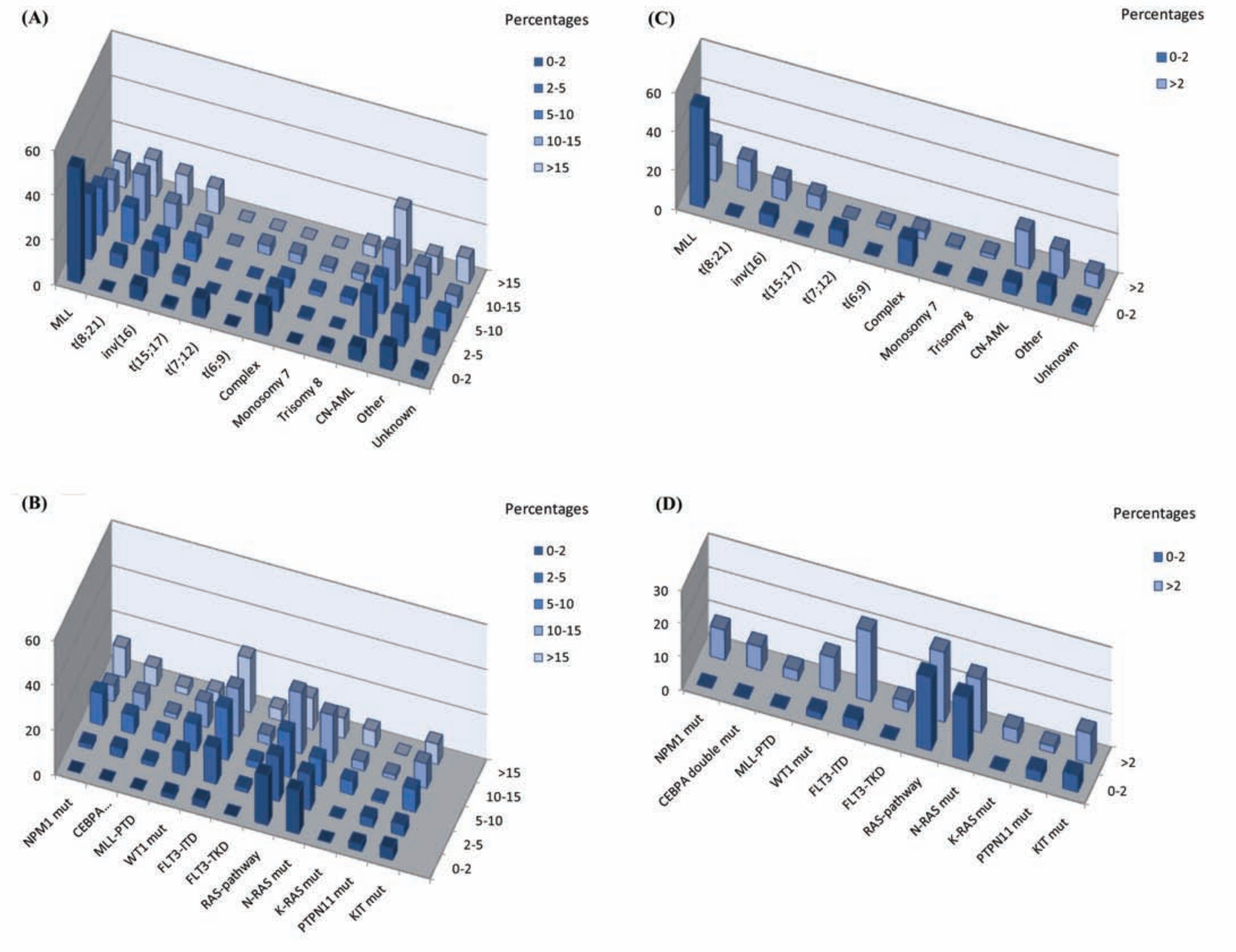
Definition of cytogenetic groups

The cytogenetic groups, i.e. 11q23/*MLL*-rearrangements, inv(16)(p13q22)/t(16;16)(p13;q22), t(8;21)(q22;q22), t(15;17)(q22;q21) and t(7;12)(q36;p13), were defined by the presence of the specific aberration, independent of accompanying aberrations. A complex karyotype was defined as the presence of 3 or more aberrations in a single clone, and without any AML-specific aberrations. Monosomy 7 and trisomy 8 were defined as the loss of chromosome 7 and a gain of chromosome 8, respectively, but without any AML-specific aberration and without a complex karyotype. The cytogenetically normal (CN-AML) group included those with a normal karyotype without any aberrations. The 'other' group included all samples not categorized in the groups mentioned above, with the exception of the 'unknown' group which included cases with failed karyotyping but without any AML-specific aberration when screened with FISH or RT-PCR.

Statistical analysis

Calculations were made using SPSS 17.0 (SPSS Inc. Chicago, USA) or SAS 9.1 (SAS Institute, Cary, NC, USA). Categorical variables were compared using χ^2 test analysis or Fisher's exact test, and the non-parametric Mann-Whitney U test was used for continuous variables. Event-free survival was determined according to events defined as failure to achieve complete remission (CR), occurrence of relapse, occurrence of secondary malignancy, or death from any cause. Probabilities of overall survival (pOS) and event-free survival (pEFS) were estimated by the Kaplan-Meier method and compared using the log rank test. Cumulative incidence of relapses (CIR) (with other events and death while in CR as competing events) were constructed by the Kalbfleisch and Prentice method and compared by Gray's test.[4] Only those groups containing more than 10 cases were included in the survival analysis; those with less than 10 cases were included in the 'other' group. Multivariate analyses were performed using Cox's proportional Hazard model. $P<0.05$ was considered significant (two-tailed).

Online Supplementary Figure S1. The different genetic aberrations according to age. Differences were found for (A) cytogenetic and (B) molecular aberrations according to age categories in pediatric AML. The most important differences were found between children older and younger than two years for (C) cytogenetic and (D) molecular aberrations.



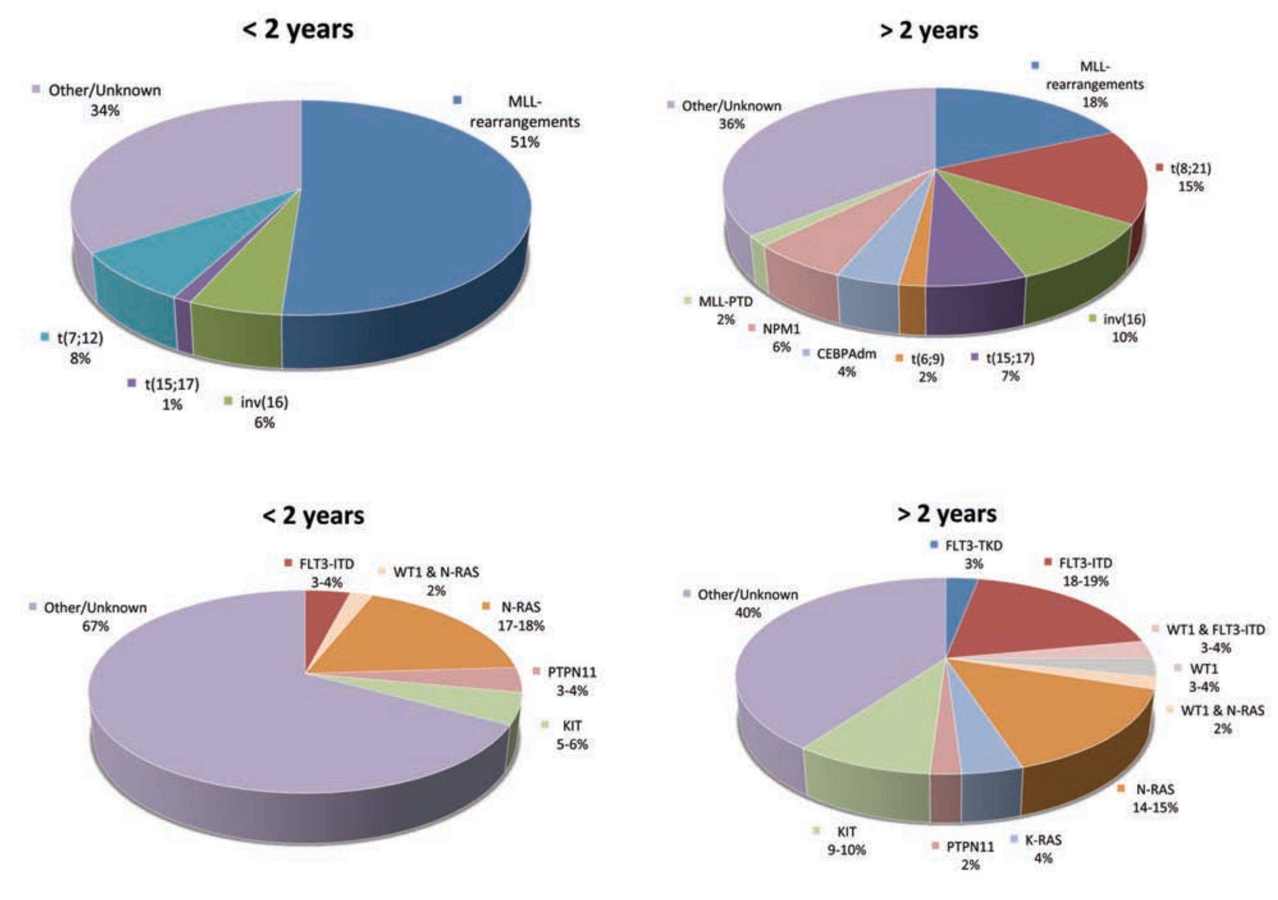


Figure 2. Distribution of the different type-I and type-II aberrations according to age. The largest differences in the frequencies of (A) type-II and (B) type-I aberrations were found between children older and younger than two years.

Online Supplementary Table S1. Hotspot regions, primers and PCR conditions for the investigated genes.

Gene*	Region / Exon	Primerpair	Primer sequences	PCR conditions***
NPM1[1]	exon 12	1598/1599	5’-CTGGTGGTAGAATGAAAAATAGAT-3’ 5’-GGCAGGGACATTCTCATAG-3’	1
CEBPA[2]	whole gene	1920/1921	5’-CGCCATGCCGGGAGAACTCT-3’ 5’-CTTGGCTTCATCCTCCTCGC-3’	2
		1922/1923	5’-CGGCCGCTGGTGATCAAG-3’ 5’-CCAGGGCGGTCCCACAGC-3’	3
MLL[3]**	specific PTD’s	1686/1687	5’-AGGAGAGAGTTTACCTGCTC-3’ 5’-GGAAGTCAAGCAAGCAGGTC-3’	1
WT1[4]	exon 7	1688/1689	5’-CATGGGGATCTGGAGTGTGA-3’ 5’-TGGGTCCTTAGCAGTGTGAGA-3’	1
	exon 9	1692/1693	5’-TAGGGCCGAGGCTAGACC-3’ 5’-TTCCAATCCCTCTCATCACAAT-3’	1
FLT3[5]	exon 14/15 (ITD)	730/731	5’-GCAATTTAGGTATGAAAGCCAGC-3’ 5’-CTTTCAGCATTTTGACGGCAACC-3’	1
	exon 20 (TKD)	719/720	5’-TCACCG GTACCTCCTACTG-3’ 5’-AAATGCACCACAGTGAGTG-3’	1
N-RAS[6]	exon 2	1635/1636	5’-GGGGGTTGCTAGAAAACTA-3’ 5’-ATCCGACAAGTGAGAGACA-3’	1
	exon 3	1637/1638	5’-CCCAGGATTCTTACAGAAAA-3’ 5’-TCCCCATAAAGATTCAGAAC-3’	1
K-RAS[6]	exon 2	1639/1640	5’-CGTCGATGGAGGAGTTT-3’ 5’-AACCCAAGGTACATTTCAGA-3’	1
PTPN11[6]	exon 3	1772/1773	5’-TTGGGTTTCTTTCAACACTT-3’ 5’-GCCTTTGGAGTCAGAGAGT-3’	1
	exon 13	1774/1775	5’-TGGCTCTGCAGTTTCTCT-3’ 5’-CATTCCGAAATCAAACAGTT-3’	1
KIT[6]	exon 8	1522/1523	5’-CCGCCTCCTTGTACCTT-3’ 5’-TTCAGCAAACAAAATTAATGTCTA-3’	4
	exon 17	1524/1525	5’-TCCTCCAACCTAATAGTGTATTC-3’ 5’-CATTCCGAAATCAAACAGTT-3’	4

*The superscript numbers refer to the below mentioned papers in which the methods were fully described.

**Positive samples were confirmed with MLPA.

***Numbers refer to the following PCR programs:

1 10’ 95°C, 40 cycles of 1’ 95°C and 1’ 60°C, 10' 72°C

2 10’ 95°C, 35 cycles of 1’ 95°C, 1’ 60°C and 1’ 72°C, 10' 72°C

3 10’ 95°C, touchdown 20 cycles of 1’ 95°C, 1’ 70-60°C and 1’ 72°C plus 20 cycles of 1’ 95°C, 1’ 60°C and 1’ 72°C, 10' 72°C

4 10’ 95°C, touchdown 20 cycles of 1’ 95°C, 1’ 66-56°C and 1’ 72°C plus 14 cycles of 1’ 95°C, 1’ 56°C and 1’ 72°C, 10' 72°C

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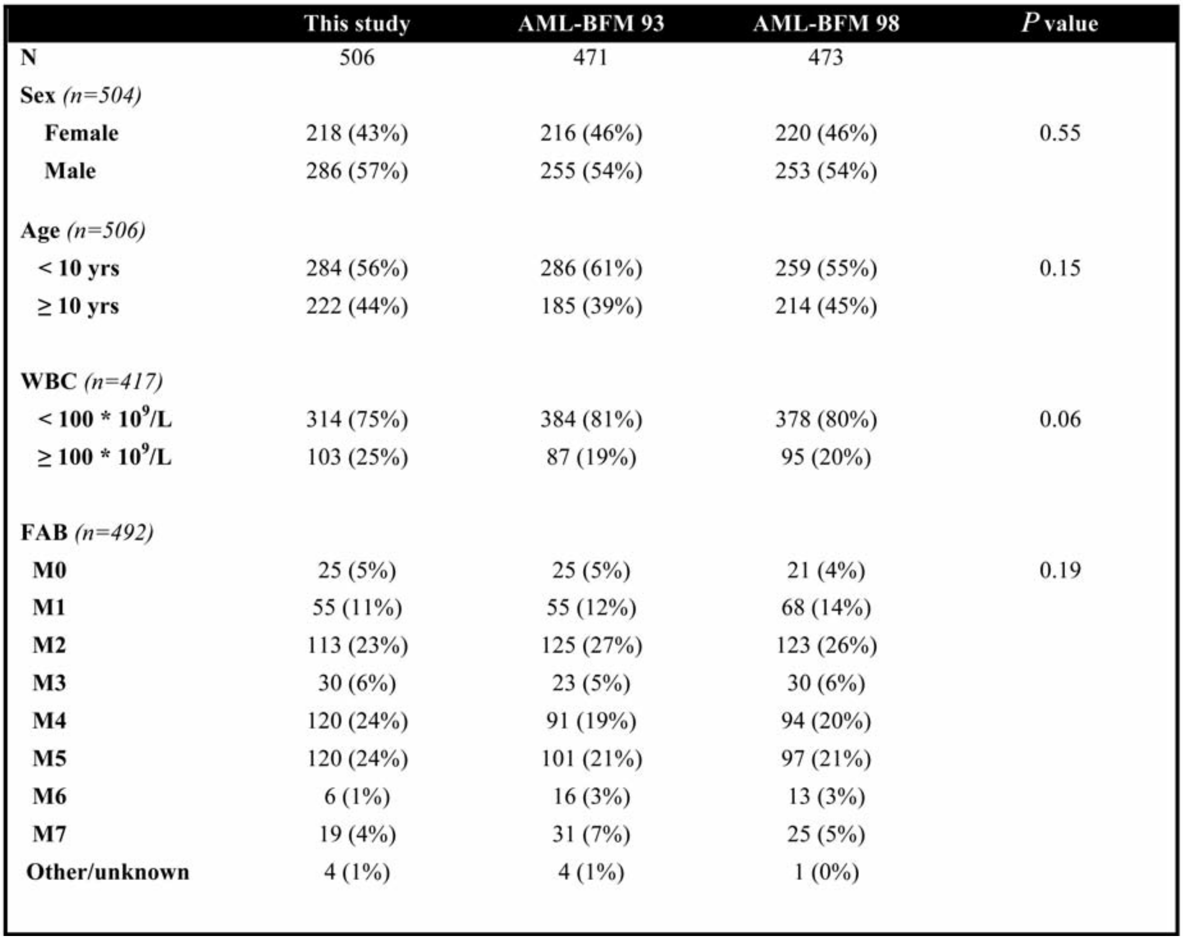
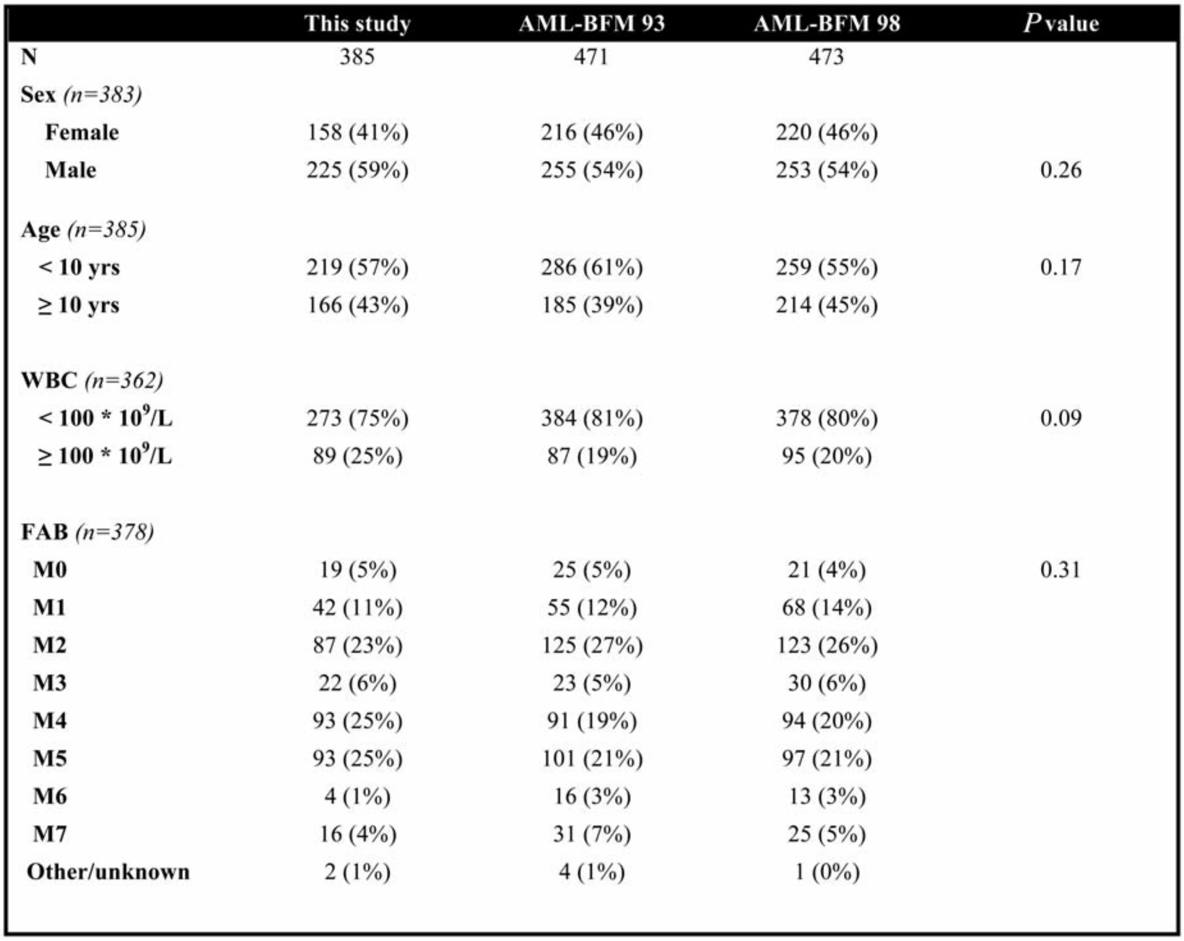
Online Supplementary Table S2. Comparison of the clinical characteristics of the total cohort (n=506) compared to the AML-BFM-93 and -98 trials, respectively.



	This study	AML-BFM 93	AML-BFM 98	*P* value
N	506	471	473	
Sex *(n=504)*				
Female	218 (43%)	216 (46%)	220 (46%)	0.55
Male	286 (57%)	255 (54%)	253 (54%)	
Age *(n=506)*				
< 10 yrs	284 (56%)	286 (61%)	259 (55%)	0.15
≥ 10 yrs	222 (44%)	185 (39%)	214 (45%)	
WBC *(n=417)*				
< 100 * 10^9/L	314 (75%)	384 (81%)	378 (80%)	0.06
≥ 100 * 10^9/L	103 (25%)	87 (19%)	95 (20%)	
FAB *(n=492)*				
M0	25 (5%)	25 (5%)	21 (4%)	0.19
M1	55 (11%)	55 (12%)	68 (14%)	
M2	113 (23%)	125 (27%)	123 (26%)	
M3	30 (6%)	23 (5%)	30 (6%)	
M4	120 (24%)	91 (19%)	94 (20%)	
M5	120 (24%)	101 (21%)	97 (21%)	
M6	6 (1%)	16 (3%)	13 (3%)	
M7	19 (4%)	31 (7%)	25 (5%)	
Other/unknown	4 (1%)	4 (1%)	1 (0%)	

Online Supplementary Table S3. Comparison of the clinical characteristics of the cases included in the survival analysis (n=385) compared to the AML-BFM-93 and -98 trials.



	This study	AML-BFM 93	AML-BFM 98	*P* value
N	385	471	473	
Sex *(n=383)*				
Female	158 (41%)	216 (46%)	220 (46%)	
Male	225 (59%)	255 (54%)	253 (54%)	0.26
Age *(n=385)*				
< 10 yrs	219 (57%)	286 (61%)	259 (55%)	0.17
≥ 10 yrs	166 (43%)	185 (39%)	214 (45%)	
WBC *(n=362)*				
< 100 * 10^9/L	273 (75%)	384 (81%)	378 (80%)	0.09
≥ 100 * 10^9/L	89 (25%)	87 (19%)	95 (20%)	
FAB *(n=378)*				
M0	19 (5%)	25 (5%)	21 (4%)	0.31
M1	42 (11%)	55 (12%)	68 (14%)	
M2	87 (23%)	125 (27%)	123 (26%)	
M3	22 (6%)	23 (5%)	30 (6%)	
M4	93 (25%)	91 (19%)	94 (20%)	
M5	93 (25%)	101 (21%)	97 (21%)	
M6	4 (1%)	16 (3%)	13 (3%)	
M7	16 (4%)	31 (7%)	25 (5%)	
Other/unknown	2 (1%)	4 (1%)	1 (0%)	

Online Supplementary Table S4. An overview of cytogenetic group assignment and the mutational status of all investigated genes of the 506 individual patients.

ID	Age (years)	Sex (F/M)	WBC ($x10^9$/l)	FAB-type	Cytogenetic group assignment	*NPM1*	*CEBPA dm**	*MLL-PTD*	*WT1*	*FLT3-ITD*	*FLT3-TKD*	*N-RAS*	*K-RAS*	*PTPN11*	*KIT*
1	2,8	M	3,7	5	MLL	0	0		0	0	0	0	0	0	0
2	0,4	M	35	5	MLL	0		0	0	0	0	0	0	0	0
3	1,6	M	129	4	MLL	0									
4	11,8	M	50	0	MLL	0	0	0	0	0	0	0	0	0	0
5	9,8	M	1,2	5	MLL	0		0		0	0	0	0	0	0
6	0,7	F	160	5	MLL	0	0	0	0	0	0	0	0	0	0
7	2,9	F	35,2	5	MLL	0	0	0	0	0	0	0	0	1	0
8	10,3	F	35,4	5	MLL	0		0		0	0	1	0	0	0
9	4,2	M	30,1	5	MLL	0	0	0	0	0	0	1	0	0	0
10	1,6	F	21,9	5	MLL	0		0		0	0	0	0	0	0
11	1,8	M	15	5	MLL	0		0							
12	1,6	M	25,2	4	MLL	0	0	0	0	0	0	0	0	0	0
13	6,9	F	200	5	MLL	0		0		0		0	0	0	0
14	7,2	M	2,3	5	MLL	0	0	0	0	0	0	0	0	0	0
15	1,6	M	16,1	5	MLL	0	0	0	0	0	0	1	0	0	0
16	14,2	M	3	5	MLL	0		0	0	0	0	0	1	0	0
17	0,3	F	NA	NA	MLL	0	0	0	0	0	0	0	0	0	0
18	1,2	M	23	7	MLL	0	0	0	0	0	0	0	0	0	0
19	7,1	F	4,8	5	MLL	0		0	0	0	0	0	0	0	0
20	1,0	M	129	4	MLL	0	0	0	0	0	0	1	0	0	0
21	1,0	M	30,1	5	MLL	0		0	0	0	0	0	0	0	0
22	9,5	F	45,7	0	MLL	0	0	0	0	1	0	0	0	0	0
23	3,5	F	13,9	4	MLL	0	0	0	0	0	0	0	0	0	0
24	11,9	F	215	2	MLL	0	0	0	0	1	0	0	0	0	0
25	8,7	M	135,4	5	MLL	0	0	0	0	0	0	0	0	0	0
26	2,0	F	13,2	5	MLL	0	0	0	0	0	0	0	0	0	0
27	2,1	M	NA	4	MLL										
28	11,2	M	358	5	MLL	0	0	0	0	0	0	0	0	0	0
29	1,3	F	14	5	MLL	0	0	0	0	0	0	0	0	0	0
30	11,1	F	108	5	MLL	0	0	0	0	0	0	0	0	0	0
31	8,7	F	585	4	MLL	0		0		0	0	0	0	0	0
32	1,1	F	175	5	MLL	0	0	0	0	0	0	0	0	0	0
33	11,5	M	104,8	5	MLL	0		0		0	0	0	0	0	0
34	16,2	M	69,7	5	MLL	0	0	0	0	0	0	1	0	0	0
35	11,2	F	42,3	5	MLL	0	0	0	0	0	0	1	0	0	0
36	0,6	M	125	5	MLL	0	0	0	0	0	0	0	0	0	0
37	7,4	M	1,1	7	MLL	0	0		0	0	0			0	
38	12,8	M	2,5	5	MLL	0	0	0	0	0	0	0	0	0	0
39	10,6	M	130	5	MLL	0	0	0	0	0	0	0	1	0	0
40	8,5	M	106	1	MLL	0		0	1	0	0	0	0	0	0
41	1,2	F	58,7	5	MLL	0				0				0	0
42	11,7	F	243,6	5	MLL	0	0	0	0	0	0	0	0	0	0
43	2,9	M	NA	5	MLL	0		0		0	0	0	0	0	0
44	0,6	F	83	5	MLL	0	0	0	0	0	0	1	0	0	0
45	0,1	F	53	5	MLL	0	0	0	0	0	0	0	0	0	0
46	0,0	M	221,2	5	MLL	0	0	0	0	0	0	0	0	0	0
47	2,3	M	23,8	5	MLL	0		0							
48	3,4	M	433	5	MLL	0	0	0	0	0	0	0	0	0	0
49	1,9	M	237	4	MLL	0	0	0	0	0	0	0	0	0	0
50	12,7	M	108	5	MLL	0	0	0	0	0	0	0	0	0	0
51	1,1	M	121,5	5	MLL	0	0	0	0	0	0	0	0	0	0
52	1,5	M	120	4	MLL	0	0	0	0	0	0	1	0	0	0
53	7,1	F	1,8	5	MLL	0		0	0	0	0	0	0	0	0
54	15,5	M	161	5	MLL	0		0		0	0	0	1	0	0
55	4,1	F	105	4	MLL	0	0	0	0	0	0	0	0	0	0

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ID	Age (years)	Sex (F/M)	WBC ($x10^9$/l)	FAB-type	Cytogenetic group assignment	*NPM1*	*CEBPA dm**	*MLL-PTD*	*WT1*	*FLT3-ITD*	*FLT3-TKD*	*N-RAS*	*K-RAS*	*PTPN11*	*KIT*
56	10,8	M	67	5	MLL	0	0	0	0	0	0	1	0	0	0
57	8,0	M	NA	4	MLL	0		0		0					
58	1,9	M	12,5	5	MLL	0	0	0	0	0	0	0	0	0	1
59	12,0	M	16,1	5	MLL	0		0		0	0	1	0	0	0
60	5,0	M	3,8	5	MLL										1
61	3,7	M	NA	4	MLL										
62	1,7	M	NA	5	MLL			0							
63	0,8	F	NA	5	MLL	0	0	0	0	0	0	1	0	0	0
64	11,1	M	NA	2	MLL							0	0		0
65	1,6	M	NA	5	MLL							0	0		0
66	14,3	M	NA	5	MLL							0	0		0
67	11,3	M	NA	5	MLL			0							
68	5,8	F	200	5	MLL	0	0	0	0	0	0	0	0	0	0
69	4,1	M	NA	0	MLL	0	0	0	0	0	0	0	0	0	0
70	5,9	M	NA	5	MLL	0	0	0	0	0	0	0	1	0	0
71	0,3	M	89	1	MLL										
72	0,4	F	68,2	2	MLL										
73	15,8	M	115	4	MLL										
74	16,9	F	93,2	1	MLL				0	0	0	0	0	0	0
75	1,4	M	330	5	MLL				0	0	0	0	0	0	0
76	0,4	M	323	4	MLL										
77	4,5	M	53,83	5	MLL	0	0	0	0	0	0	1	0	0	0
78	14,6	M	468,8	5	MLL	0	0	0	0	0	0	0	0	0	0
79	8,1	M	143	1	MLL	0	0	0	0	0	0	0	0	0	0
80	9,8	M	83	5	MLL	0	0	0	0	0	0	0	1	0	0
81	1,7	F	40,6	5	MLL	0	0	0	0	0	0	0	0	0	0
82	0,6	F	6	5	MLL		0	0	0	0	0	0	0	0	0
83	1,4	F	7,1	5	MLL		0	0	0	0	0	0	0	0	0
84	14,1	F	3,1	5	MLL										
85	2,7	F	17,1	5	MLL		0	0		0	0	0	0	0	0
86	7,6	M	129	5	MLL				0	0	0	1	0	0	0
87	17,3	M	25,7	4	MLL	0			0	0	0	0	0	0	0
88	6,5	M	48,9	5	MLL	0				0					
89	2,2	M	94,81	5	MLL										
90	0,4	M	167	5	MLL	0			0	0	0	0	0	0	0
91	12,4	M	106	0	MLL				0	0	0	0	1	0	0
92	1,1	F	284	5	MLL					0					
93	16,7	F	52,7	4	MLL	0			0	0	0	0	0	0	1
94	0,8	F	475	4	MLL	0			0	0	0	0	0	0	0
95	0,6	F	136	5	MLL	0			0	0	0	0	0	0	0
96	2,0	M	289	5	MLL	0	0		0	0	1	0	0	0	0
97	9,0	M	225	0	MLL				0	0	0	0	1	0	0
98	1,3	M	7,3	5	MLL										
99	2,5	M	22,7	5	MLL										
100	12,2	F	NA	NA	MLL										
101	3,7	F	4	5	MLL				0	0	0	0	0	0	0
102	1,6	F	49,8	5	MLL				0	0	0	0	0	0	0
103	4,0	F	NA	0	MLL				0	0	0	1	0	0	0
104	0,7	F	NA	4	MLL				0	0	0	1	0	0	0
105	0,4	F	394	5	MLL				0	0	0	1	0	0	0
106	5,3	M	34	5	MLL			0	0						0
107	4,9	F	NA	5	MLL										
108	14,6	M	NA	5	MLL					0		0	0	0	0
109	0,8	M	NA	5	MLL										
110	1,9	M	NA	5	MLL										
111	2,0	M	16,2	5	MLL										
112	3,7	F	6,6	5	MLL					0		0	0	0	0
113	6,6	F	184,8	5	MLL					0		0	0	0	0

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ID	Age (years)	Sex (F/M)	WBC ($x10^9/l$)	FAB-type	Cytogenetic group assignment	*NPM1*	*CEBPA dm**	*MLL-PTD*	*WT1*	*FLT3-ITD*	*FLT3-TKD*	*N-RAS*	*K-RAS*	*PTPN11*	*KIT*
114	6,1	F	170,4	5	MLL					0		0	0	0	0
115	6,3	M	NA	4	MLL					0		0	0	0	1
116	0,1	M	NA	4	MLL					0		1	0		0
117	15,8	M	NA	0	MLL					0		0	0	0	0
118	1,4	M	NA	5	MLL										
119	2,0	M	6,5	4	MLL					0		0	0	0	0
120	1,8	M	16,3	7	MLL										
121	0,7	M	NA	5	MLL					0		0	0	0	0
122	4,0	F	NA	5	MLL	0		0		0	0	0	0	0	0
123	6,0	M	22,7	NA	t(8;21)										
124	8,1	M	12,8	2	t(8;21)										
125	13,1	M	4,6	2	t(8;21)	0	0	0	0	0	0	0	0	0	0
126	9,9	M	8,2	2	t(8;21)	0	0	0	0	0	0	0	0	0	1
127	5,5	M	35,5	4	t(8;21)	0	0	0	0	0	0	1	0	0	0
128	10,0	M	9,1	2	t(8;21)	0		0	0	0	0			0	0
129	6,2	F	11,6	1	t(8;21)	0		0							0
130	16,7	F	7,1	4	t(8;21)	0	0	0	0	0	0	0	0	0	0
131	8,6	M	46,7	2	t(8;21)	0	0	0	0	0	0	0	0	0	1
132	15,4	M	11,5	2	t(8;21)	0		0							0
133	10,0	M	32,8	2	t(8;21)	0	0	0	0	1	0	0	0	0	0
134	9,6	M	20	2	t(8;21)	0		0							0
135	14,6	M	37,4	2	t(8;21)	0	0	0	0	0	0	0	0	0	1
136	15,0	M	20,4	2	t(8;21)	0	0	0	0	0	0	0	0	0	1
137	15,0	M	12,8	NA	t(8;21)	0	0	0	0	0	0	0	0	0	0
138	15,3	M	2,8	2	t(8;21)	0	0	0	0	0	0	0	0	0	0
139	8,8	M	5,9	2	t(8;21)		0		0	0	0				1
140	15,2	M	50,5	2	t(8;21)	0	0	0	0	0	0	0	0	0	1
141	12,9	F	4,1	2	t(8;21)	0		0		0	0	0	0	0	0
142	11,0	M	7,8	2	t(8;21)	0	0	0	0	0	1	1	0	0	0
143	13,4	F	2,3	1	t(8;21)	0	0	0	0	0	0	0	0	0	1
144	8,3	F	24,5	4	t(8;21)	0	0	0	0	0	0	0	0	0	0
145	14,2	M	23,5	2	t(8;21)										0
146	7,9	F	10	2	t(8;21)										
147	14,4	M	19	2	t(8;21)	0	0	0	0	0	0	1	0	0	0
148	3,6	M	10,4	2	t(8;21)	0	0	0	0	0	0	0	0	0	0
149	4,3	F	12,5	2	t(8;21)	0	0	0	0	0	0	0	0	0	0
150	10,3	M	13,6	2	t(8;21)	0	0	0	0	0	0	0	0	0	0
151	14,2	M	13,9	2	t(8;21)										1
152	14,3	M	320	2	t(8;21)	0	0	0	0	0	0	0	0	0	0
153	14,4	M	33,8	2	t(8;21)	0	0	0	0	1	0	0	0	0	0
154	5,5	F	17,4	4	t(8;21)				0	0	0	0	0	0	1
155	9,3	M	NA	2	t(8;21)										
156	11,2	M	NA	2	t(8;21)										
157	6,9	M	NA	2	t(8;21)										
158	4,5	F	NA	2	t(8;21)										
159	13,9	F	12,9	2	t(8;21)					0					
160	2,6	F	35,5	2	t(8;21)				0	0		0	0	0	1
161	6,1	M	9,9	2	t(8;21)				0	0		0	0	0	0
162	9,7	M	9	2	t(8;21)				0	0	0	0	0	0	0
163	12,5	F	24	2	t(8;21)				0	0		0	0	0	1
164	16,6	F	3,8	2	t(8;21)					0					
165	9,1	F	17,9	2	t(8;21)				0	0		0	0	0	0
166	12,7	F	7,1	2	t(8;21)				0	0		0	0	0	1
167	13,2	F	17,1	2	t(8;21)					0					
168	14,6	M	9	2	t(8;21)	0	0	0	0	0	0	0	1	0	0
169	13,9	F	10,7	2	t(8;21)	0	0	0	0	0	0	0	0	0	0
170	16,8	F	2	2	t(8;21)	0	0	0	0	0	0	0	0	0	0
171	10,6	M	21,8	2	t(8;21)	0	0	0	0	0	0	0	0	0	1

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ID	Age (years)	Sex (F/M)	WBC ($x10^9/l$)	FAB-type	Cytogenetic group assignment	*NPM1*	*CEBPA dm**	*MLL-PTD*	*WT1*	*FLT3-ITD*	*FLT3-TKD*	*N-RAS*	*K-RAS*	*PTPN11*	*KIT*
172	11,0	M	9,1	2	t(8;21)		0	0	0	0	0	0	0	0	1
173	14,2	F	20,5	2	t(8;21)										
174	15,7	M	36,5	2	t(8;21)										
175	12,4	F	24,4	2	t(8;21)										
176	7,0	F	13,5	2	t(8;21)	0	0	0	0	0	1	0	0	0	0
177	14,1	F	41,3	4	t(8;21)	0	0	0	0	0	0	1	0	0	0
178	13,9	F	NA	2	t(8;21)			0							0
179	10,9	M	7,4	2	t(8;21)										0
180	11,7	M	33	2	t(8;21)										
181	18,5	F	10,5	2	t(8;21)										
182	10,9	M	8,39	2	t(8;21)	0				0					
183	14,3	F	24	2	t(8;21)	0			0	0	0	0	0	0	0
184	3,8	M	NA	2	t(8;21)										
185	10,4	F	NA	2	t(8;21)										
186	13,7	F	NA	2	t(8;21)										
187	2,0	M	66,8	4	inv(16)	0	0	0	0	0	0	0	0	0	1
188	12,9	F	233,5	4	inv(16)	0	0	0	0	0	0	0	0	0	1
189	7,2	M	68,3	4	inv(16)	0	0	0	0	0	0	0	0	0	0
190	0,7	F	84,8	4	inv(16)	0	0	0	0	0	0	0	0	0	1
191	15,8	M	180	4	inv(16)	0	0	0	0	0	0	0	1	0	0
192	8,2	F	68,9	4	inv(16)	0		0		0					
193	8,0	F	40,2	4	inv(16)	0	0	0	0	0	0	1	0	0	0
194	1,9	M	22	4	inv(16)	0	0	0	0	0	0	0	0	0	0
195	15,8	M	114	4	inv(16)	0	0	0	0	0	0	0	0	0	1
196	12,8	M	33	4	inv(16)	0	0	0	0	0	0	1	0	0	0
197	12,6	F	99,0	4	inv(16)	0	0	0	0	0	0	0	0	0	1
198	4,5	M	10,1	4	inv(16)	0	0	0	0	0	0	0	0	0	0
199	13,0	F	43,6	4	inv(16)	0	0	0	0	0	0	1	0	0	0
200	3,3	M	219	4	inv(16)	0	0	0	0	0	0	0	0	0	0
201	9,8	F	10,2	4	inv(16)	0	0	0	0	0	0	0	0	0	0
202	10,7	M	4,4	4	inv(16)	0	0	0	0	0	0	0	0	0	0
203	12,6	M	4,3	4	inv(16)	0	0	0	0	0	0	1	0	0	0
204	2,8	M	108	4	inv(16)	0	0	0	0	0	0	0	0	0	0
205	12,4	M	49,3	4	inv(16)	0	0	0	0	0	0	0	0	0	0
206	16,4	F	18,3	4	inv(16)										0
207	5,7	M	4,9	4	inv(16)										
208	10,2	M	NA	5	inv(16)				0	0	0	1	0	0	1
209	10,3	F	77,1	4	inv(16)	0	0	0	0	0	0	0	0	0	1
210	15,9	F	74,8	2	inv(16)	0	0	0	0	0	0	0	0	0	0
211	13,3	M	NA	4	inv(16)				0	0	0	0	0	0	1
212	4,0	M	47,3	4	inv(16)	0	0	0	0	0	0	0	0	0	1
213	0,8	F	NA	4	inv(16)										
214	12,2	F	NA	4	inv(16)										
215	13,6	F	NA	4	inv(16)										
216	16,9	M	NA	4	inv(16)	0	0	0	0	0	0	1	1	0	0
217	4,6	F	NA	4	inv(16)										
218	2,7	M	76,7	4	inv(16)				0	1		0	0	0	0
219	13,8	M	88,1	4	inv(16)				0	0	0	0	0	0	0
220	13,6	M	94,9	4	inv(16)				0	0	0	0	0	0	1
221	5,5	F	85,4	4	inv(16)				0	0	0	0	1	0	0
222	14,5	F	3	4	inv(16)	0	0	0	0	0	0	0	0	0	0
223	15,0	M	106,8	2	inv(16)	0	0	0	0	0	0	0	0	0	0
224	5,4	M	32,8	4	inv(16)	0	0	0	0	0	0	0	0	0	1
225	17,3	F	142	4	inv(16)	0	0	0	0	0	0	0	0	0	0
226	1,6	M	29,5	4	inv(16)	0	0	0	0	1	0	0	0	0	0
227	3,3	M	NA	2	inv(16)			0							0
228	2,0	M	97	4	inv(16)										0
229	16,6	F	91	4	inv(16)				0	0	1	0	0	0	0

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ID	Age (years)	Sex (F/M)	WBC (x10^9/l)	FAB-type	Cytogenetic group assignment	*NPM1*	*CEBPA dm**	*MLL-PTD*	*WT1*	*FLT3-ITD*	*FLT3-TKD*	*N-RAS*	*K-RAS*	*PTPN11*	*KIT*
230	14,4	M	202,9	4	inv(16)	0				0					
231	13,5	F	109	4	inv(16)	0			0	0		0	0	1	0
232	1,9	F	20,1	4	inv(16)	0			1	0	0	1	0	0	0
233	7,9	F	22,8	4	inv(16)	0			0	0	0	0	0	0	0
234	13,0	F	10,3	4	inv(16)										
235	10,8	F	218	3	t(15;17)	0	0		0	1	0	0	0	0	0
236	15,9	M	2,6	3	t(15;17)										
237	8,7	M	2,9	3	t(15;17)										
238	7,1	M	24,4	NA	t(15;17)	0	0	0	0	0	0	0	0	0	0
239	4,2	M	29	1	t(15;17)				0	0	0	0	0	1	0
240	11,5	M	1,2	2	t(15;17)	0	0	0	0	0	0	0	0	0	0
241	11,4	M	107	3	t(15;17)	0	0	0	0	1	0	0	0	0	0
242	4,1	F	14,5	3	t(15;17)	0	0	0	0	0	0	0	0	0	0
243	1,9	M	58,7	3	t(15;17)	0	0	0		1					
244	15,2	F	NA	3	t(15;17)	0	0	0	0	1	0	0	0	0	0
245	10,1	M	NA	3	t(15;17)	0	0	0	0	1	0	0	0	0	0
246	10,2	F	NA	3	t(15;17)										
247	2,0	M	205	3	t(15;17)				0	1	0	0	0	0	0
248	15,6	F	53,8	3	t(15;17)				0			0	0	0	0
249	7,0	F	71	3	t(15;17)	0	0	0	0	1	0	0	0	0	0
250	11,9	F	6,7	3	t(15;17)	0	0	0	1	0	1	0	0	0	0
251	8,7	M	27,5	3	t(15;17)	0	0	0	0	1	0	0	0	0	0
252	15,1	F	7,3	3	t(15;17)	0	0	0	0	1	0	0	0	0	0
253	7,3	M	4,5	3	t(15;17)	0	0	0	0	0	0	0	0	0	0
254	9,4	F	246,8	3	t(15;17)	0	0	0	0	1	0	0	0	0	0
255	16,9	M	18,1	3	t(15;17)	0	0	0	0	0	1	0	0	0	0
256	14,7	F	8,1	3	t(15;17)	0	0	0	0	1	0	0	0	0	0
257	5,3	M	60	3	t(15;17)			0							
258	17,7	F	18	3	t(15;17)	0	0	0	0	0	0	0	0	0	0
259	15,1	F	41,6	3	t(15;17)	0	0	0	0	1	0	0	0	0	0
260	14,7	F	22,5	3	t(15;17)	0	0	0	0	1	0	0	0	0	0
261	9,5	F	81,5	3	t(15;17)	0	0	0	0	1	0	0	0	0	0
262	9,8	F	NA	3	t(15;17)										
263	0,2	F	217,9	2	t(7;12)					0	0	0	0	0	1
264	1,5	M	226,8	3	t(7;12)	0	0	0	0	0	0	0	0	0	0
265	1,1	F	21,8	7	t(7;12)	0	0	0	0	0	0	0	0	0	0
266	0,3	F	88,8	0	t(7;12)	0	0	0	0	0	0	0	0	0	0
267	0,3	F	21,1	0	t(7;12)					0	0	0	0	0	0
268	0,3	M	14	1	t(7;12)				0	0	0	0	0	0	0
269	0,6	F	NA	0	t(7;12)					0	0	0	0	1	0
270	14,4	M	85,2	5	t(6;9)	0	0	0	1	1	0	0	0	0	0
271	10,3	M	120,2	4	t(6;9)	0	0	0	1	0	0	0	0	0	0
272	12,6	M	107,1	2	t(6;9)	0	0	0	0	0	0	0	0	0	0
273	14,9	M	NA	4	t(6;9)	0	0	0	0	0	0	1	0	0	0
274	11,8	F	NA	2	t(6;9)	0	0	0	0	1	0	0	0	0	0
275	12,8	F	NA	2	t(6;9)	0	0	0	0	0	0	1	0	0	0
276	13,7	F	24,4	4	t(6;9)										
277	1,3	M	8,4	7	complex (>3)	0									
278	1,6	F	20	1	complex (>3)	0		0							
279	14,1	M	42	5	complex (>3)	0	0	0	0	0	0	0	0	0	0
280	14,4	F	74	4	complex (>3)	0		0							
281	0,1	F	16	7	complex (>3)										
282	14,3	M	320	0	complex (>3)	0	0	0	1	0	1	0	0	0	0
283	0,9	M	5,6	7	complex (>3)	0	0		0	0	0	0	0	0	0
284	7,3	M	81,2	1	complex (>3)	0	0		0	0	0	0	0	0	0
285	4,8	F	22,6	bilineage	complex (>3)	0	0		0	1	0	0	0	0	0
286	3,0	F	NA	7	complex (>3)										
287	1,4	F	14,9	7	complex (>3)	0	0	0	0	0	0	0	0	0	0

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ID	Age (years)	Sex (F/M)	WBC (x10^9/l)	FAB-type	Cytogenetic group assignment	*NPM1*	*CEBPA dm**	*MLL-PTD*	*WT1*	*FLT3-ITD*	*FLT3-TKD*	*N-RAS*	*K-RAS*	*PTPN11*	*KIT*
288	8,5	F	2,9	4	complex (>3)	0	0	0	0	0	0	0	0	0	0
289	1,8	M	11,5	7	complex (>3)	0	0	0	0	0	0	0	0	0	0
290	1,4	F	19	NA	complex (>3)	0	0	0	0	0	0	0	0	0	0
291	3,9	M	NA	2	complex (>3)										
292	2,1	F	47,6	7	complex (>3)	0	0	0	0	0	0	0	0	0	0
293	2,8	F	NA	5	complex (>3)										
294	2,1	M	NA	NA	complex (>3)	0	0	0	0	0	0	0	0	0	0
295	11,0	M	NA	1	complex (>3)				0	0	0	1	0	0	0
296	0,6	F	66,9	4	complex (>3)										
297	6,4	M	9,1	1	complex (>3)										
298	2,0	F	21	7	complex (>3)										
299	1,2	M	23,9	6	complex (>3)										
300	13,5	F	8,6	2	complex (>3)	1	0	0	0	0	0	0	0	0	0
301	5,9	M	155,9	5	complex (>3)	0	0		0	0	0	0	1		0
302	4,8	M	13,7	5	complex (>3)										
303	0,6	M	31,6	7	complex (>3)	0	0	0	0	0	0	0	0	0	0
304	1,5	M	16,5	0	complex (>3)				0	0					
305	11,2	M	97,1	bilineage	complex (>3)										
306	1,3	F	NA	7	complex (>3)										
307	10,9	F	54,9	4	monosomy 7	0	0	0	0	0	0	0	0	0	0
308	9,6	M	66	2	monosomy 7	0	1	0	0	0	0	1	0	0	0
309	12,2	M	NA	4	monosomy 7		0	0	0	0	0	0	0	0	0
310	14,1	F	NA	4	monosomy 7	0	0	0	0	0	0	1	0	0	0
311	4,2	M	NA	4	monosomy 7										
312	5,0	M	3,4	1	monosomy 7	0	0			0					
313	16,7	M	100	5	trisomy 8										
314	15,1	M	154,4	5	trisomy 8	0	0	0	0	1	0	0	0	0	0
315	14,9	M	302	4	trisomy 8	0		0							
316	7,3	F	54,6	5	trisomy 8	0	0	0	1	1	0	0	0	0	0
317	8,2	F	34,3	2	trisomy 8	0	0	0	0	0	0	0	0	0	0
318	1,0	M	NA	5	trisomy 8	0	0	0	0	0	0	0	0	0	0
319	16,8	M	NA	6	trisomy 8										
320	11,2	M	NA	2	trisomy 8										
321	14,3	F	NA	1	trisomy 8			0							
322	12,7	M	160	5	trisomy 8	0	0		0	1	0	0	0	0	0
323	9,9	F	35,2	2	trisomy 8	0				0					
324	1,4	M	7,8	7	trisomy 8			0	0						0
325	10,4	M	332	4	CN	0	0	0	1	1	0	0	0	0	0
326	0,1	F	32	4	CN	0	0	0	0	0	0	0	0	0	0
327	2,3	M	15	4	CN	0	0	0	1	0	0	1	0	0	0
328	5,8	M	86	2	CN	0	1	0	1	0	0	0	0	0	0
329	9,7	F	9,5	1	CN	1	0	0	0	0	0	0	0	0	0
330	7,8	F	50,1	1	CN	1	0	0	0	1	0	0	0	0	0
331	3,6	M	21,3	2	CN	1	0	0	0	0	0	1	0	0	0
332	3,6	M	14,1	2	CN	0		0							
333	3,7	M	38	5	CN	0	0	0	0	0	0	0	0	0	0
334	4,0	M	33,9	2	CN	0	0	0	1	1	0	0	0	0	0
335	10,0	F	534,6	2	CN	0	0	0	0	1	0	0	0	0	0
336	15,6	M	388,3	2	CN	0	1	0	0	1	0	0	0	0	0
337	14,9	M	57,1	NA	CN	0	0	0	0	1	0	0	0	0	0
338	11,2	F	96	2	CN	0	0	0	0	1	0	0	0	0	0
339	9,0	F	92,9	4	CN	0	0	0	0	1	0	0	0	0	0
340	11,1	F	163	4	CN	1	0	0	0	1	0	0	0	0	0
341	11,2	F	72,9	2	CN	0	0	1	0	0	1	0	0	0	0
342	5,0	M	98	2	CN										
343	2,7	M	7,3	4	CN										
344	4,1	M	7,4	4	CN	0	0	0	1	0	0	1	0	0	0
345	7,6	M	5,3	4	CN	0	0	0	0	0	0	1	0	0	0

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ID	Age (years)	Sex (F/M)	WBC ($x10^9/l$)	FAB-type	Cytogenetic group assignment	*NPM1*	*CEBPA dm**	*MLL-PTD*	*WT1*	*FLT3-ITD*	*FLT3-TKD*	*N-RAS*	*K-RAS*	*PTPN11*	*KIT*
346	15,3	M	30,8	4	CN	1	0	0	0	0	0	1	0	0	0
347	6,6	F	2,4	mixed lineage	CN	0	0	0	0	0	0	0	0	0	0
348	6,9	F	25,1	4	CN	0	0	0	0	0	0	1	0	0	0
349	11,0	F	48,2	1	CN	1	0	0	0	1	0	0	0	0	0
350	9,6	M	58	2	CN	1	0	0	0	1	0	0	0	0	0
351	7,5	M	120,4	1	CN	0	0	1	0	1	0	0	0	0	0
352	17,8	M	189	2	CN	0	0	0	1	1	0	0	0	0	0
353	0,8	F	42,2	5	CN	0	0	0	0	0	0	1	0	0	0
354	15,2	M	289	4	CN										
355	7,9	M	310	1	CN										
356	2,8	F	193,4	2	CN										
357	6,2	M	324	2	CN	0	0	0	1	1	0	0	0	0	0
358	16,5	F	73,9	2	CN	1	0	0	0	1	0	1	0	0	0
359	8,4	F	8,2	2	CN	0	1	0	0	0	0	0	0	0	0
360	14,7	M	33,8	4	CN	1	0	0	0	1	0	0	0	0	0
361	15,3	F	22	2	CN										
362	12,6	F	48	0	CN	0	0	0	1	0	0	1	0	0	0
363	12,6	F	140,6	5	CN	0	0	0	1	1	0	0	0	0	0
364	12,3	F	22	2	CN	1	0	0	0	0	0	1	0	0	0
365	11,9	M	39,7	2	CN	0	0	0	0	1	0	1	0	0	0
366	12,6	M	32,8	1	CN	0	1	0	0	0	0	0	0	0	0
367	4,1	M	377,6	1	CN	0	0	0	0	1	0	0	0	0	0
368	14,3	F	44,8	1	CN	0	0	1	0	1	0	0	0	0	0
369	11,9	M	7,7	0	CN	0	0	0	0	0	0	0	0	0	0
370	2,4	M	267,3	4	CN	0	0	0	0	1	0	0	0	0	0
371	0,7	M	8,2	5	CN	0	0	0	0	0	0	0	0	1	0
372	13,2	F	6,3	2	CN	0	1	0	0	0	0	0	0	0	0
373	14,6	F	NA	2	CN										
374	15,1	M	NA	2	CN	0	0	0	0	0	0	0	0	0	0
375	12,4	M	NA	4	CN	0	0	0		0	0	1	0	0	0
376	14,0	M	NA	1	CN										
377	11,0	M	71	5	CN	1	0	0	0	0	0	0	0	0	0
378	1,1	M	NA	7	CN										
379	3,0	M	NA	5	CN										
380	6,9	F	NA	NA	CN										
381	4,0	M	354	1	CN	0	1	0	1	0	0	1	0	0	0
382	14,6	F	140	2	CN	0	1	0	1	0	0	0	0	0	0
383	10,3	F	119	1	CN	0	1		0	0	0	0	0	0	0
384	13,2	M	14,9	4	CN	1	0	0	0	1	0	0	0	0	0
385	7,9	M	2,3	3	CN										
386	4,7	F	15,6	4	CN	0	0	0	0	0	0	0	0	0	0
387	15,4	F	230	1	CN	1	0	0	0	0	0	0	0	0	0
388	15,1	M	4,9	1	CN	0	0	0		1					
389	16,8	F	187	1	CN	0	0	0	1	1	0	0	0	0	0
390	12,6	F	3,4	2	CN	0	0	0	0	0	0	0	0	0	0
391	13,0	M	226	1	CN	0	0	0	0	1	0	0	0	0	0
392	18,5	M	43,1	2	CN	0	1	0	0	0	0	0	0	0	0
393	14,8	F	16	4	CN	1	0	0	0	0	0	1	0	0	0
394	18,8	F	61,1	2	CN	1	0	0	0	1	0	0	0	0	0
395	12,3	M	57,2	3	CN	0	0	0	1	1	0	0	0	0	0
396	8,4	M	25	1	CN	0	0	0	1	1	0	0	0	0	0
397	2,3	M	153	4	CN	0	0	0	0	1	0	0	0	0	0
398	0,8	F	32,1	4	CN	0	0	0	0	0	0	0	0	0	0
399	15,7	F	9,54	1	CN	0	1	0	0	0	0	0	0	0	0
400	14,3	M	2,2	2	CN	0				0					
401	15,3	M	1,3	4	CN	0			0	0		0	0	0	0
402	2,7	M	384	4	CN	0			0	0		0	0	0	0
403	6,0	M	NA	1	CN	1	0	0	0	1	0	0	0	0	0

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ID	Age (years)	Sex (F/M)	WBC (x10^9/l)	FAB-type	Cytogenetic group assignment	*NPM1*	*CEBPA dm**	*MLL-PTD*	*WT1*	*FLT3-ITD*	*FLT3-TKD*	*N-RAS*	*K-RAS*	*PTPN11*	*KIT*
404	17,0	F	NA	1	CN	0	0	0	0	0	0	0	0	0	0
405	14,9	M	NA	2	CN	0	0	0	0	0	0	1	0	0	0
406	5,1	M	NA	4	CN	0	0	0	1	1	1	0	0	0	0
407	15,3	M	1,4	6	CN	0	0	0	0	0	0	0	0	0	0
408	3,1	M	9,5	2	CN	0	0	0	1	0	0	0	0	0	0
409	7,4	F	58,1	5	other	0		0							
410	0,4	F	7,2	5	other										
411	0,6	M	73	5	other	0	0	0	0	0	0	0	0	0	0
412	0,1	M	32,6	5	other										
413	4,3	M	3,1	4	other										
414	0,1	F	10,1	7	other										
415	7,7	M	5,2	4	other	1	0	0	0	0	0	0	0	0	0
416	0,0	F	157	6	other	0	0		0	0	0	0	0	0	0
417	9,0	M	2,5	2	other	0	0	0	1	0	0	0	0	0	0
418	14,0	M	12,4	2	other	0	0	0	0	0	0	1	0	0	0
419	5,2	F	42,9	1	other	1	0	0	0	1	0	0	0	0	0
420	12,0	M	78,8	1	other	0	1	0	0	0	0	0	0	0	0
421	2,6	M	17,4	5	other	0	0	0	0	0	0	0	0	0	0
422	6,3	M	196	0	other	0	0	0	1	0	0	1	0	0	0
423	14,6	F	2,2	1	other	0		0	0	0					
424	14,6	F	15	5	other	0	0	0	0	0	0	1	0	0	0
425	9,1	F	4,4	5	other	0	0	0	0	0	0	0	0	1	0
426	12,9	F	214	4	other	0	0	0	1	0	0	0	0	0	0
427	13,8	M	6,5	0	other	0	0	0	0	0	0	0	0	0	0
428	7,0	M	68,1	1	other	0	0	1	0	0	0	1	0	0	0
429	0,0	M	223	5	other				0	0		0	0	0	0
430	14,8	F	54	1	other	0	1	0	0	0	0	0	0	0	0
431	4,8	F	50,9	4	other	0									
432	5,2	M	15,9	0	other										
433	10,0	F	452	4	other	0		0							
434	16,6	F	7,6	NA	other	0									
435	10,4	M	10	2	other	0	0	0	0	0	0	0	0	0	0
436	13,9	M	NA	4	other	0	0	0	0	0	0	0	0	0	0
437	14,4	M	151	5	other	0	0	0	0	0	0	0	0	0	0
438	2,3	M	39,9	5	other										
439	9,2	F	45,2	5	other	0	0	0	1	0	0	0	0	0	0
440	6,2	M	30	0	other	0	0		0	1	0	0	0	0	0
441	3,9	F	19,8	1	other	0	0	0	0	0	0	0	0	0	0
442	4,0	F	24	1	other	0	1		0	0	0	0	0	0	0
443	9,7	M	2,4	0	other	0	0	0	0	0	0	0	0	0	0
444	14,2	M	5	4	other	0	0	0	0	0	0	0	0	0	0
445	9,6	M	121,3	4	other	0	0	0	0	1	0	0	0	0	0
446	4,9	M	20	0	other	0	0	0	0	0	0	0	0	0	0
447	15,9	F	108	4	other	1		0		0	0	0	0		
448	6,9	F	181,5	1	other	0	1	0	0	1	0	0	0	0	0
449	3,8	F	7,8	1	other	0	0	0	0	0	0	0	0	0	0
450	14,0	F	NA	NA	other	0	0	0	1	1	0	0	0	0	0
451	8,4	F	NA	1	other	0	0	0	0	0	0	0	0	0	0
452	14,1	F	NA	NA	other										
453	15,2	F	NA	5	other										
454	13,2	F	NA	5	other										
455	10,3	F	NA	0	other	0	0	0	0	0	0	0	0	0	0
456	13,0	M	NA	2	other										
457	8,8	F	NA	1	other	0	1	0	0	1	0	0	0	0	0
458	5,7	M	NA	1	other										
459	3,4	M	87,2	NA	other	0	0	0	0	0	0	0	0	0	0
460	15,0	F	75,8	4	other	0	0		0	0	0	0	0	0	0
461	2,3	M	28,6	4	other	0	0	0	0	0	0	0	0	0	0

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ID	Age (years)	Sex (F/M)	WBC (x10^9/l)	FAB-type	Cytogenetic group assignment	*NPM1*	*CEBPA dm**	*MLL-PTD*	*WT1*	*FLT3-ITD*	*FLT3-TKD*	*N-RAS*	*K-RAS*	*PTPN11*	*KIT*
462	18,4	M	4,5	2	other	1	0	0	0	0	0	0	0	0	0
463	0,5	F	288,31	4	other	0	0		0	0	0	1	0	0	0
464	3,4	F	148	1	other	0			0	1		0	0	0	0
465	12,8	M	115	1	other	0	0		0	0	0	1	0	1	0
466	7,3	M	95	4	other			0	0						0
467	10,7	NA	NA	1	other					0					
468	13,8	F	43,9	4	other										
469	11,5	F	1,3	5	other										
470	2,9	M	7,6	0	other										
471	0,6	M	4	5	other										
472	14,3	M	7,8	4	other										
473	1,2	M	9,5	7	other										
474	0,7	F	7,5	5	unknown										
475	3,9	M	483	1	unknown	0	0	0	0	0	0	1	0	0	0
476	13,4	F	6	2	unknown	0	1	0	0	0	0	0	0	0	0
477	1,1	M	1,5	5	unknown	0		0						0	
478	5,4	M	23,3	1	unknown	1	0	0	0	0	0	0	0	0	0
479	14,1	M	1,7	0	unknown	0	0	0		0	0	0	0	0	0
480	11,3	F	NA	5	unknown	0	0	0	1	0	0	0	1	0	0
481	4,8	F	NA	0	unknown	0	0	1	0	0	0	0	0	0	0
482	13,7	F	13,8	2	unknown										
483	15,9	F	1,4	3	unknown	0									
484	15,3	M	47,5	1	unknown	0		0							
485	7,5	NA	169,9	4	unknown	0		1		1					
486	14,3	F	3,4	1	unknown										
487	14,3	M	56,5	2	unknown										
488	6,9	F	39,3	2	unknown	1		0		0	0	0	0		
489	2,9	M	11,5	mixed lineage	unknown										
490	9,4	M	NA	2	unknown										
491	0,8	M	105	5	unknown	0	0	0	0	0	0	0	0	0	0
492	9,0	M	46,7	2	unknown	1	0	0	0	0	0	1	0	0	0
493	2,0	F	168	6	unknown	0	0	0	0	0	0	1	0	0	0
494	5,1	M	14,8	7	unknown	0	0	0	0	0	0	0	0	0	0
495	14,6	M	168,3	2	unknown										
496	4,9	M	31,4	6	unknown	0	0	0	0	0	0	0	0	0	0
497	7,1	F	85,1	NA	unknown	1	0	0	0	0	0	0	0	0	0
498	15,5	M	NA	4	unknown										
499	18,0	M	NA	4	unknown	0	0	1	0	1	0	0	0	0	0
500	13,6	F	NA	1	unknown	0	0	0	0	0	0	0	0	0	0
501	8,5	F	NA	0	unknown			0							
502	3,9	M	64	2	unknown	0	0			1					
503	16,7	F	0	5	unknown										
504	15,1	M	52,7	3	unknown	0	0	0	0	0	0	0	0	0	0
505	6,4	F	102,7	1	unknown	1			0	0		0	0	0	1
506	15,4	F	35	1	unknown	0	0		0	0	0	0	0	0	0

F = female, M = male, NA = not available; 1 = positive, 0 = negative, and blank indicates not screened.

** CEBPAdm indicates presence of a CEBPA double mutation; single mutations are counted as negative.*

Online Supplementary Table S5. Overview of the association between type-I and type-II aberrations in pediatric AML.

	Type-I aberrations*								
	FLT3-ITD (n=372)			FLT3-TKD (n=330)			KIT (n=368)		
Type-II aberrations	mutation (%)	mutation (n)	wild type (n)	mutation (%)	mutation (n)	wild type (n)	mutation (%)	mutation (n)	wild type (n)
MLL-rearrangements	3	2	93	1	1	80	4	4	92
t(8;21)	5	2	40	6	2	31	31	14	31
inv(16)	5	2	37	3	1	34	28	11	29
t(15;17)	64	14	8	10	2	19	-	0	22
t(7;12)	-	0	7	-	0	7	14	1	6
t(6;9)	33	2	4	-	0	6	-	0	6
NPM1 mut	39	10	16	-	0	25	4	1	23
CEBPA double mut	18	3	14	-	0	17	-	0	17
MLL-PTD	57	4	3	17	1	5	-	0	6
Other/unknown type-II**	25	28	83	2	2	97	-	0	105
Overall	18	67	305	3	9	321	8	31	337

	N-RAS (n=353)			K-RAS (n=353)			PTPN11 (n=330)		
Type-II aberrations	mutation (%)	mutation (n)	wild type (n)	mutation (%)	mutation (n)	wild type (n)	mutation (%)	mutation (n)	wild type (n)
MLL-rearrangements	18	17	76	8	7	86	1	1	90
t(8;21)	11	4	32	3	1	35	-	0	37
inv(16)	19	7	30	8	3	34	3	1	36
t(15;17)	-	0	22	-	0	22	5	1	21
t(7;12)	-	0	7	-	0	7	14	1	6
t(6;9)	33	2	4	-	0	6	-	0	6
NPM1 mut	23	6	20	-	0	26	-	0	24
CEBPA double mut	12	2	15	-	0	17	-	0	17
MLL-PTD	17	1	5	-	0	6	-	0	6
Other/unknown type-II**	18	18	85	2	2	101	3	3	100
Overall	16	57	296	4	13	340	2	7	343

	WT1 (n=330)***		
Type-II aberrations	mutation (%)	mutation (n)	wild type (n)
MLL-rearrangements	1	1	71
t(8;21)	-	0	37
inv(16)	3	1	36
t(15;17)	5	1	21
t(7;12)	-	0	4
t(6;9)	33	2	4
NPM1 mut	-	0	24
CEBPA double mut	18	3	14
MLL-PTD	-	0	6
Other/unknown type-II**	20	21	84
Overall	9	29	301

* *type-I aberrations were mutually exclusive, except for FLT3-ITD & N-RAS (n=2), FLT3-TKD & N-RAS (n=1), KIT & N-RAS (n=1), N-RAS & PTPN11 (n=1) and N-RAS & K-RAS (n=1).*

** *the following numbers were screened for molecular type-II aberrations in the other/unknown type-II group: CEBPA (n=101/180), NPM1 (n=118/180) and MLL-PTD (n=101/180).*

***WT1 *mutations overlap with* FLT3/ *ITD (n=12),* FLT3/ *TKD (n=3),* N-RAS *(n=6) and* K-RAS *(n=1).*