LETTER TO THE EDITOR

Deciphering the molecular complexity of the IKZF1^{plus} genomic profile using Optical Genome Mapping

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Supplemental Data

Table S1 Overview of patient characteristics is provided for patients with *IKZF1* wildtype (IKZF1^{WT}), *IKZF1* deletion (IKZF1^{del}), and IKZF1^{plus}. WBC: white blood cell; CNS: central nervous system; Pred. resp.: Prednison response; MRD: minimal residual disease; SR: standard risk; MR: medium risk; HR: high risk; n/a: not available.

	IKZF1^{WT}		IKZF1^{del}		IKZF1^{plus}		p(Fisher) IKZF1$^{del/plus}$
	N	**%**	**N**	**%**	**N**	**%**	
All	843	100	71	100	64	100	
Sex							0.230
Male	446	52.9	44	62.0	33	51.6	
Female	397	47.1	27	38.0	31	48.4	
Age							0.165
Age <10 years	663	78.6	35	49.3	40	62.5	
Age ≥10 Years	180	21.4	36	50.7	24	37.5	
WBC							0.101
WBC $<10^4$	383	45.4	18	25.4	8	12.5	
WBC 10^4-$<5\times10^4$	308	36.5	31	43.7	24	37.5	
WBC 5×10^4-$<10^5$	91	10.8	12	16.9	18	28.1	
WBC $\geq10^5$	61	7.2	10	14.1	14	21.9	
CNS							0.311
n/a	36	4.3	4	5.6	2	3.1	
negativ	786	93.2	64	90.1	56	87.5	
positiv	21	2.5	3	4.2	6	9.4	
ETV6::RUNX1							0.059
n/a	40	4.7	2	2.8	0	0.0	
negativ	585	69.4	64	90.1	64	100	
positiv	218	25.9	5	7.0	0	0.0	
Hyperdiploid							0.115
n/a	170	20.2	7	9.9	1	1.6	
negativ	515	61.1	58	81.7	62	96.9	
positiv	158	18.7	6	8.5	1	1.6	
Down Syndrome							0.190
No	824	97.7	70	98.6	60	93.8	
Yes	19	2.3	1	1.4	4	6.3	
Pred.resp.							0.122
n/a	3	0.4	2	2.8	0	0.0	
Pred. Good	788	93.5	57	80.3	59	92.2	
Pred. Poor	52	6.2	12	16.9	5	7.8	
Risiko MRD							0.146
n/a	134	15.9	7	9.9	4	6.3	
MRD: 1-2 neg.	338	40.1	13	18.3	21	32.8	
MRD: other	343	40.7	33	46.5	28	43.8	
MRD: 2 $\geq10^{-3}$	28	3.3	18	25.4	11	17.2	
Risk group							0.072
SR 2000	329	39	11	15.5	20	31.3	
MR 2000	437	51.8	32	45.1	27	42.2	
HR 2000	77	9.1	28	39.4	17	26.6	

Table S2 Overview of the identified gene fusions, their corresponding breakpoints, and the allocation to specific subgroups. Gene fusions were categorized into distinct groups (*ABL*-class, *CRLF2*, *JAK2*, PAX5, *ZNF384*, and other fusions. Among patients with gene fusions 20 were assigned to the IKZF1^{del} and 33 to the IKZF1^{plus}. Sanger sequencing was employed for breakpoint validation.

Fusion Class	*Fusion*	*Count*	*Type*	*Breakpoints*	*Subgroup*
ABL-class	*EBF1::PDGFRB*	2	Deletion	e15::e11	IKZF1^{del}
	ETV6::ABL1	1	Insertion	not validated	IKZF1^{plus}
	FIP1L1::PDGFRA	1	Deletion	e13:e12	IKZF1^{del}
	NUP153::ABL1	1	Translocation	e11::e4	IKZF1^{del}
	RCSD1::ABL1	1	Translocation	e3::e4	IKZF1^{del}
	RSCD1::ABL2	3	Inversion, complex insertion	e3::e5	1 IKZF1^{del} 2 IKZF1^{plus}
	ZC3HAV1::ABL2	2	Translocation	e12::e2	IKZF1^{del}
	ZMIZ1::ABL1	1	Insertion	e18::e2	IKZF1^{del}
CRLF2	*P2RY8::CRLF2*	12	Deletion	e1::e1	IKZF1^{plus}
JAK2	*ATF7IP::JAK2*	1	Translocation	e13:e19	IKZF1^{plus}
	EBF1::JAK2	1	Translocation	e14::e17	IKZF1^{plus}
	NPAT::JAK2	1	Translocation	e10::e18[25]	IKZF1^{del}
	PAX5::JAK2	5	Inversion, complex variant	4 e4::e19 1 e5::19	4 IKZF1^{del} 1 IKZF1^{plus}
	PRPF4B::JAK2	1	Translocation	e8::e19	IKZF1^{plus}
	TERF2::JAK2	1	Translocation	e9::e19	IKZF1^{del}
PAX5	*PAX5::AUTS2*	4	Translocation, complex variant	1 e6::e4 2 e6::e5 1 e8::e7	1 IKZF1^{del} 3 IKZF1^{plus}
	PAX5::DACH1	1	Complex variant	e8::e4	IKZF1^{plus}
	PAX5::ELK3	1	Translocation	e7::e2	IKZF1^{plus}
	PAX5::ETV6	1	Translocation	e4::e3	IKZF1^{plus}
	PAX5::FOXP1	1	Translocation	e5::e12	IKZF1^{plus}
	PAX5::NOL4L	1	Translocation	e7::e11	IKZF1^{plus}
ZNF384	*EWSR1::ZNF384*	1	Translocation	e13::e2	IKZF1^{plus}
	SMARCA4::ZNF384	1	Insertion	e4::e2	IKZF1^{del}
	TAF15::ZNF384	1	Translocation	e11::e3	IKZF1^{del}
	TCF3::ZNF384	1	Translocation	e5::e3	IKZF1^{plus}
other	*ASXL1::HRNPA2B1*	1	Translocation	e4::e10	IKZF1^{plus}
	DNMT3B::ZCCHC7	1	Translocation	e21::e6	IKZF1^{plus}
	NFE2L3::ETV6	1	Translocation	e3::e3, e2::e3	IKZF1^{plus}
	TCF3::PBX1	1	Translocation	not validated	IKZF1^{del}
	UBTF::ATXN7L3	2	Deletion	e17::5'UTR	IKZF1^{plus}

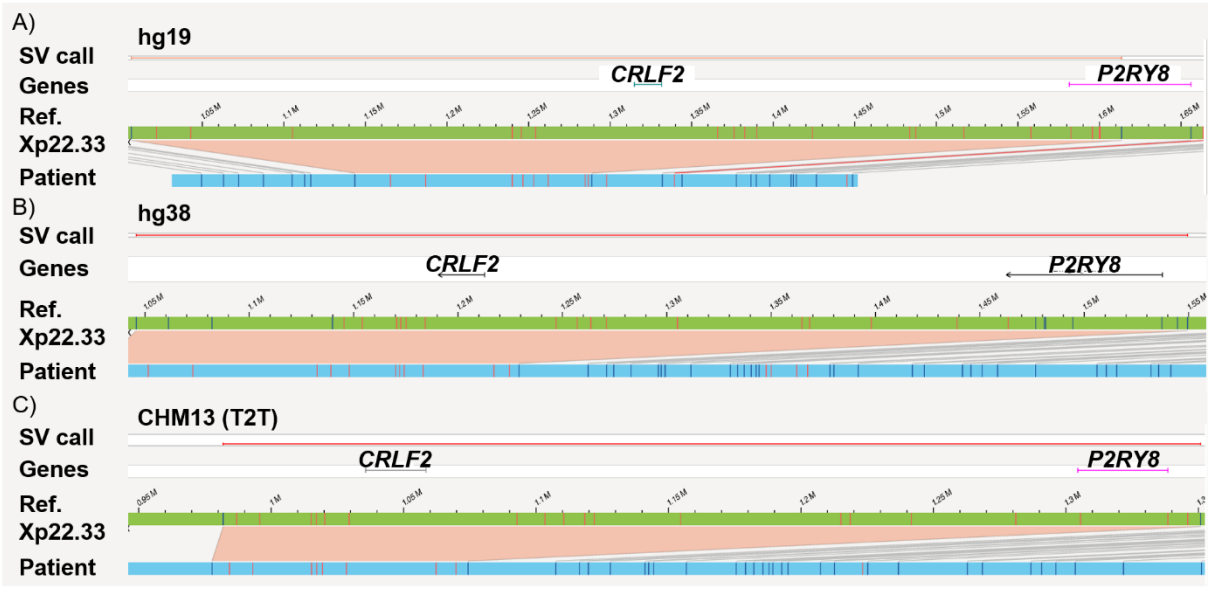

Figure S1 Optical Genome Mapping results for the PAR1 deletion at Xp22.33 aligned to different reference genomes. The on Xp22.33 from the identical patient was aligned to A) hg19 reference, B) hg38 reference, and C) CHM13 (T2T). The assessment of the deletion was becoming more accurate when using the more recent reference genomes. The reference map is depicted in green and the patient map is represented in light blue.