Supplementary Table S3: Summary of the advanced molecular characterization performed in the analysed samples

PATIENT ID	DISEASE	STATUS	KARYOTYPE[1]	REARRAN-GEMENTS	CNAs	GENE OVEREX-PRESSION	VARIANTS IDENTIFIED BY NGS	PANEL VERSION	% BLASTS	VAF	DEPTH	AMP CLASS	TIER
HRL 1	MPL	D	complex	*E2A-other*	Del. in *CDKN2A/B*, and *GBE1*. Dup. in *EBF1*.	*WT1*	***FLT3*** NM_004119.2:c.2516A>G(p.Asp839Gly) ***FLT3*** NM_004119.2:c.2503G>T(p.Asp835Tyr)	v.2	55	0.09 0.18	1098x 1101x	LO O	1 D 1 T
HRL 2	B-ALL	R	normal	N/A	-	NO	***KRAS*** NM_004985.4:c.34G>T(p.Gly12Cys) ***NT5C2*** NM_012229.4:c.1100G>A(p.Arg367Gln)	v.1	12	0.13 0.07	516x 676X	O LO	2 T 2 P
HRL 3	B-ALL	R	complex	NO	Del. in *CDKN2A/B*, *PAX5*, *MLLT3*, *MTAP*. Dup. in *ABL1* and *NUP214*.	NO	***PTPN11*** NM_002834.4:c.205G>A(p.Glu69Lys)	v.2	33	0.10	1501x	O	2 D
HRL 4	B-ALL	D	normal	NO	-	-	NO	v.1	88	-	-	-	-
HRL 4	B-ALL	r	normal	NO	Del. in *CDKN2A/B*, and *IKZF1*.	*CRLF2*	NO	v.1	52	-	-	-	-
HRL 5	T-ALL	R	N/A	N/A	-	-	***FBXW7*** NM_018315.4:c.1273C>T(p.Arg425Cys) ***NOTCH1*** NM_017617.4:c.5033T>C(p.Leu1678Pro) ***AKT1*** NM_001014432.1:c.49G>A(p.Glu17Lys)	v.1	19	0.06 0.06 0.07	1274x 901x 1366x	O LO O	1 P 1 P 2 T
HRL 6	B-ALL	R	hypodiploid	NO	-	-	NO	v.2	2	-	-	-	-
HRL 7	AML	D	normal	NO	-	*WT1*	***FLT3*** NM_004119.2:c.2503_2506delinsC, p.Asp835_Ile836delinsLeu ***WT1*** NM_024426.4:c.1372C>T(p.Arg458*)	v.2	50	0.35 0.42	1175x 1325x	O LO	1 T 1 P
HRL 7	AML	R	normal	NO	-	*WT1*	***FLT3*** NM_004119.2:c.2503_2506delinsC, p.Asp835_Ile836delinsLeu ***WT1*** NM_024426.4:c.1372C>T(p.Arg458*)	v.2	70	0.89 0.95	823x 1018x	O LO	1 T 1 P
HRL 8	AML	R	normal	NO	-	-	NO	v.2	35	-	-	-	-
HRL 9	T-ALL	D	normal	NO	-	-	***PTEN*** NM_000314.6:c.737_738insTGAA(p.Leu247fs) ***PTEN*** NM_000314.6:c.388C>G(p.Arg130Gly)	v.1	84	0.06 0.66	1037x 1017x	LO O	2 T 2 T
HRL 9	T-ALL	R	normal	NO	Del. in *CDKN2A/B*, *MLLT3*, *MTAP* and *PTEN*.	*CRLF2*	***PTEN*** NM_000314.6:c.388C>G(p.Arg130Gly)	v.2	71	0.59	884x	O	2 T
HRL 10	B-ALL	D	normal	NO	-	-	***PTPN11*** NM_002834.4:c.226G>A(p.Glu76Lys)	v.2	78	0.29	108x	O	2 D
HRL 10	B-ALL	r	normal	NO	Del. in *PAX5*, *IKZF1*, *CDKN2A/B*.	*CRLF2*	***PTPN11*** NM_002834.4:c.226G>A(p.Glu76Lys) ***KMT2D*** NM_003482.3:c.15289C>T(p.Arg5097*)	v.2	65	0.28 0.05	289x 905x	O O	2 D 2 D
HRL 11	AML	R	normal	NO	-	*WT1*	***WT1*** NM_024426.4:c.1137_1141dupACGGT(p.Ser381fs) ***KMT2D*** NM_003482.3:c.1349_1350insAA(p.Pro451fs) ***FLT3*** NM_004119.2:c.1779_1832dup(p.Glu611fs)[2]	v.2	40	0.29 0.20 -	1180x 1728x -	LO LO O	1 P 2 D 1 T
HRL 12	B-ALL	R	N/A	N/A	-	-	***KRAS*** NM_004985.4:c.38G>A(p.Gly13Asp) ***ATRX*** NM_000489.4:c.4868T>G(p.Leu1623*)	v.2	100	0.50 0.97	373x 281x	O LO	2 T 2 D
HRL 13	B-ALL	R	normal	NO	Del. in *IKZF1*, *BTG1* and X chromosome.	NO	NO	v.2	60	-	-	-	-

HRL 14	B-ALL	D	normal	*KMT2A-MLLT1 (MLL1-ENL)*	No CNVs	NO	NO	v.2	90	-	-	-	-
HRL 14	B-ALL	R	normal	*KMT2A-MLLT1 (MLL1-ENL)*	No CNVs	NO	***MPL*** NM_005373.2:c.1642delG(p.Ala548fs)	v.2	59	0.13	399x	LO	2 D
HRL 15	B-ALL	R	hyperdiploid	*ETV6-RUNX1*	Del. in *ETV6.*	NO	NO	v.2	40	-	-	-	-
HRL 16	T-ALL	R	hyperdiploid	NO	Del. in *CDKN2A/B* locus (*MTAP, PHF6*). Dup. in *AHI1.*	NO	***PHF6*** NM_032458.2:c.903C>A(p.Tyr301*) ***WT1*** NM_024426.4:c.1128_1129insGGATATCG(p.Thr377fs)	v.2	54	0.68 0.28	1266x 1539x	LO LO	1 D 2 P
HRL 17	B-ALL	D	normal	*E2A-other*	-	-	***SUZ12*** NM_015355.3:c.456-2A>T ***NRAS*** NM_002524.4:c.183A>C(p.Gln61His) ***NRAS*** NM_002524.4:c.38G>A(p.Gly13Asp)	v.2	58	0.06 0.19 0.07	301x 1365x 1589x	LO O O	2 D 2 T 2 T
HRL 17	B-ALL	r	normal	*E2A-other*	Del. in *PAX5* and *CDKN2A/B.*	NO	***NRAS*** NM_002524.4:c.183A>C(p.Gln61His)	v.2	65	0.28	1884x	O	2 T
HRL 18	B-ALL	D	normal	*BCR-ABL1*	Del. in *JAK2* and *PAX5.* Dup. in *SHOX, CRLF2* and *CSF2RA.*	NO	NO	v.2	65	-	-	-	-
HRL 19	B-ALL	R	hyperdiploid	*ETV6-RUNX1*	Del. in *ETV6.* Dup. in *SHOX* and *CRLF2*.	NO	NO	v.2	60	-	-	-	-
HRL 20	B-ALL	R	N/A	N/A	Del. in *CDKN2A.* Dup. in *PAX5.*	NO	***KRAS*** NM_004985.4:c.191_192insTGTTAACCAGTA(p.Tyr64_Ser65insValAsnGlnTyr)	v.1	88	0.19	317x	LO	2 T
HRL 21	B-ALL	D	hyperdiploid	NO	-	NO	***NRAS*** NM_002524.4:c.181C>A(p.Gln61Lys)	v.1	95	0.40	226x	O	2 T
HRL 22	B-ALL	D	normal	*BCR-ABL1*	-	-	NO	v.1	81	-	-	-	-
HRL 22	B-ALL	R	normal	*BCR-ABL1*	-	NO	NO	v.2	42	-	-	-	-
HRL 23	B-ALL	R	N/A	N/A	Del. in *IKZF1.*	NO	NO	v.1	93	-	-	-	-
HRL 24	B-ALL	R^1	hyperdiploid	NO	-	-	***PTPN11*** NM_002834.4:c.182A>T(p.Asp61Val) ***MSH6*** NM_000179.2:c.402dupT(p.Asp135fs) ***CREBBP*** NM_004380.2:c.4506G>C(p.Trp1502Cys) ***NT5C2*** NM_012229.4:c.713G>A(p.Arg238Gln)	v.2	81	0.37 0.09 0.38 0.25	1790X 2430X 4155X 976X	O LO LO LO	2 D 2 P 2 D 2 P
HRL 24	B-ALL	R^2	normal	NO	-	-	***PTPN11*** NM_002834.4:c.182A>T(p.Asp61Val) ***CREBBP*** NM_004380.2:c.4506G>C(p.Trp1502Cys) ***CDKN2A*** NM_058195.3:c.319dupC(p.His107fs) ***NT5C2*** NM_012229.4:c.713G>A(p.Arg238Gln)	v.2	84	0.42 0.46 0.08 0.46	713x 636x 1106x 856x	O LO LO LO	2 D 2 D 2 T 2 P

HRL 25	B-ALL	D	normal	*KMT2A-other*	No CNVs	NO	NO	v.2	90	-	-	-	-
HRL 25	B-ALL	R	normal	NO	No CNVs	NO	NO	v.2	60	-	-	-	-
HRL 26	T-ALL	D	normal	NO	No CNVs	-	***PHF6*** NM_032458.2:c.121_122insTCCCTTCTTCCTCG(p.Ala41fs) ***PTEN*** NM_000314.6:c.696dupA(p.Arg233fs) ***PTEN*** NM_000314.6:c.740T>C(p.Leu247Ser)	v.2	77	0.41 0.35 0.33	299x 1389x 1580x	LO LO O	1 D 2 T 2 T
HRL 26	T-ALL	R	hyperdiploid	NO	No CNVs	*CRLF2*	***PHF6*** NM_032458.2:c.121_122insTCCCTTCTTCCTCG(p.Ala41fs) ***PTEN*** NM_000314.6:c.696dupA(p.Arg233fs)	v.2	87	0.44 0.88	637x 1855x	LO LO	1 D 2 T

ID: Identity; CVAs: Copy Number Alterations; NGS: Next Generation Sequencing; VAF: Variant Allele Frequency; MPL: Mixed Phenotype Acute Leukaemia; B-ALL: B-cell-precursor Acute Lymphoblastic Leukaemia; T-ALL: T-cell-precursor Acute Lymphoblastic Leukaemia; AML: Acute Myeloid Leukaemia; D: diagnosis; R: relapsed; r: refractory; Del.: deletion; Dup.: duplication; LO: Likely Oncogenic; O: Oncogenic; P: prognostic; T: therapeutic; 1: first relapse; 2: second relapse

[1] Karyotype: Hyperdiploid karyotype is considered if ≥47 chromosomes and hypodiploid if ≤ 45 chromosomes. Complex karyotype is defined by the presence of ≥3 cytogenetic alterations.

[2] VAF and depth are available for SNPs and indels, but not for internal tandem duplications (ITD)