Genetic and genomic analysis of acute lymphoblastic leukemia in older adults reveals a distinct profile of abnormalities: analysis of 210 patients from the UKALL14 and UKALL60+ clinical trials

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SUPPLEMENTARY DATA

Supplementary methods

Patients, samples and outcome data

All patients aged 60 years and over that had been enrolled into 2 large multi-centre clinical trials were first identified. UKALL14 (NCT01085617) was a phase 3 randomised controlled trial that recruited patients aged 25-65 years (or 19-65 years if *BCR-ABL1* positive) with newly diagnosed ALL between 30/12/2010 and 26/07/2018. Patients were treated with intensive multi-agent chemotherapy, followed by allogeneic stem cell transplantation in first remission where indicated according to risk stratification and donor availability. UKALL60+ (NCT01616238) was a phase 2 trial that recruited patients aged ≥60 years at diagnosis (or ≥55 years if deemed unfit for more intensive treatment) between 29/01/2013 and 26/11/2018. Treatment protocols ranged from intensive multi-agent chemotherapy to low intensity palliative regimens. All patients with *BCR-ABL1* positive disease received imatinib together with either intensive multi-agent (UKALL14) or low intensity (UKALL60+) chemotherapy.

Event-free survival (EFS) was defined as time to relapse, second tumour or death, censoring at date of last contact. Relapse rate (RR) was defined as time to relapse for those achieving a complete remission, censoring at date of death in remission or last contact. Overall survival (OS) was defined as time to death, censoring at date of last contact. All survival rates are quoted at 5 years. Kaplan-Meier methods were used to estimate survival rates and the two-sided log-rank test was employed to evaluate the equality of the survivorship functions in different subgroups.

B-other ALL cases

B-other ALL refers to a heterogenous subgroup of patients who lack a primary chromosomal abnormality by conventional cytogenetic techniques. Specifically, these included cases with normal, failed or complex karyotypes or those without subgroup-

defining chromosomal abnormalities. Failed karyotypes were required to have had *BCR-ABL1* and *KMT2A* fusions excluded by fluorescence in situ hybridisation (FISH).

ABL1 break apart FISH (Cytocell, Cambridge, UK) was also performed in cases where the *BCR-ABL1* dual colour dual fusion pattern had identified in extra *ABL1* signal, potentially suggesting a variant *ABL1* rearrangement. All FISH patterns were interpreted by two independent observers with a minimum of 100 nuclei scored and an abnormal pattern was reported if detected in at least 10% of nuclei by both observers.

Preparation of SNP array data

Copy number segmentation and visualisation were carried out using Nexus Copy Number 10 (Biodiscovery, El Segundo, CA).

Raw array data from Affymetrix (Santa Clara, CA, USA) arrays were loaded directly to Nexus Copy Number 10 (Biodiscovery, El Segundo, CA, USA) in the form of CEL files. Illumina (San Diego, CA, USA)-generated IDAT files first needed to be converted into a text-based format before being loaded to Nexus. To achieve this, the Illumina-specific SNP array software package – GenomeStudio 2.0 – was used, in accordance with the Nexus protocol for the analysis of Illumina arrays. The IDAT files were loaded to GenomeStudio 2.0 and then converted into text-based format by creating a Final_Report file. This was then loaded onto Nexus to visualise the data and perform copy number segmentation.

Systematic correction of the arrays was then performed. This is a recommended step in the analysis of SNP array data due to the waviness in the probe signals that can often be seen across the genome[1]. This is partly related to GC content as probes with high GC content will bind better to their target sequence, producing a higher signal intensity. As such, systematic correction was performed in Nexus using the recommended Illumina and Affymetrix correction files.

Nexus employs a hybrid segmentation algorithm termed Fast Adaptive States Segmentation Technique (FASST2). This is based on HMM-segmentation but does not assume fixed integer levels of copy number, and instead accepts a large number of potential copy number states falling between fixed integer levels.

To account for the variation in probe density between the array platforms, a minimum of 10 probes was required for copy number segments with Affymetrix arrays and 6 probes with Illumina arrays. Constitutional copy number variations were excluded by discarding segments with ≥50% overlap with regions reported in the Toronto Database of Genomic Variants. CNAs smaller than 10kb and those that did not contain any genes were also excluded.

Next generation sequencing (NGS) analyses

Separately, regions that contained the breakpoints of selected gene deletions identified by SNP array were also included in the capture library to validate novel abnormalities by a second technique.

BAM files were deduplicated and re-aligned to the reference genome (GRCh37/hg19). Variant calling of single nucleotide variants (SNVs) and indels was performed using GATK HaplotypeCaller and Ensembl VEP (supplementary methods). Deletion breakpoints were confirmed by directly examining sequencing reads using the Integrative Genomics Viewer (IGV) (21) and identifying mate pairs that spanned the deletion breakpoint.

A SureSelect XT2 capture library (Agilent, Santa Clara, CA, USA) was designed using the SureDesign web portal (https://earray.chem.agilent.com/suredesign/) to capture either exons or the full sequence of genes implicated in leukaemogenesis (supplementary table 1). DNA samples were first amplified using a REPLI-g mini kit (Qiagen, Hilden, Germany) to yield at least 1 ug of whole genome amplified DNA. Following amplification, double stranded DNA concentrations were measured using the Quant-iT Picogreen broad-range assay (Invitrogen, Carlsbad, CA, USA) and FLUOstar Omega microplate reader (BGM Labtech, Ortenberg, Germany). SureSelect XT2 libraries were then prepared using 1 ug of input DNA. Mechanical DNA shearing was performed on the Bioruptor pico sonication system (Diagenode, Liège, Belgium) inputting shearing settings as follow – time on: 7 seconds; time off: 90 seconds; number of cycles: 4 – to yield 800-1000 bp fragments. Sample quality and fragment size were then assessed on the 2100 Bioanalyzer (Agilent) to ensure that a fragment peak was visible around 800-1000 bp. Library prep was then performed according to the manufacturer's protocol with two exceptions: i) the ratio of AMPure

XP beads (Beckman Coulter, Brea, CA, USA): DNA was reduced to 0.7 to optimise bead-binding to the longer DNA fragments in the library and ii) The PCR amplification was performed using the Longamp Taq polymerase enzyme (New England Biolabs, Ipswich MA, USA), which is optimized for amplification of longer DNA fragments.

Each pooled library was sequenced using a mid-output kit on the Illumina NextSeq 550 with 100bp paired end reads. BAM files were generated and then deduplicated and re-aligned to the reference genome (hg19/GRCh37). As no germline DNA was available, variant calling was performed using the GATK HaplotypeCaller[3]. Ensembl VEP files were produced and calls with a population allele frequency ≥0.01 in the Exome Aggregation Consortium (ExAC) database[4] were excluded as likely germline variants. All non-coding variants, synonymous variants, and those reported as both tolerated and benign in the SIFT[5] and Polyphen[6] databases respectively were also excluded. Calls with COSMIC identifiers were examined in the COSMIC database[7] to identify known somatic mutations in cancer, specifically those in *TP53*.

Supplementary references

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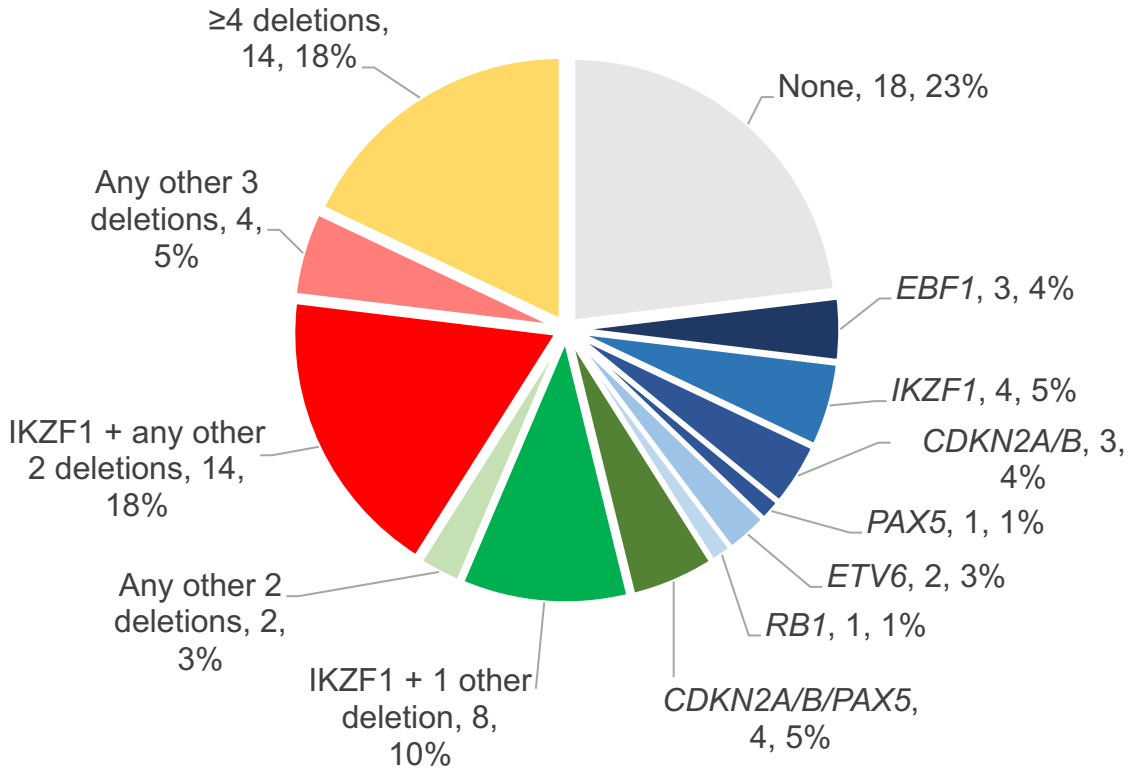
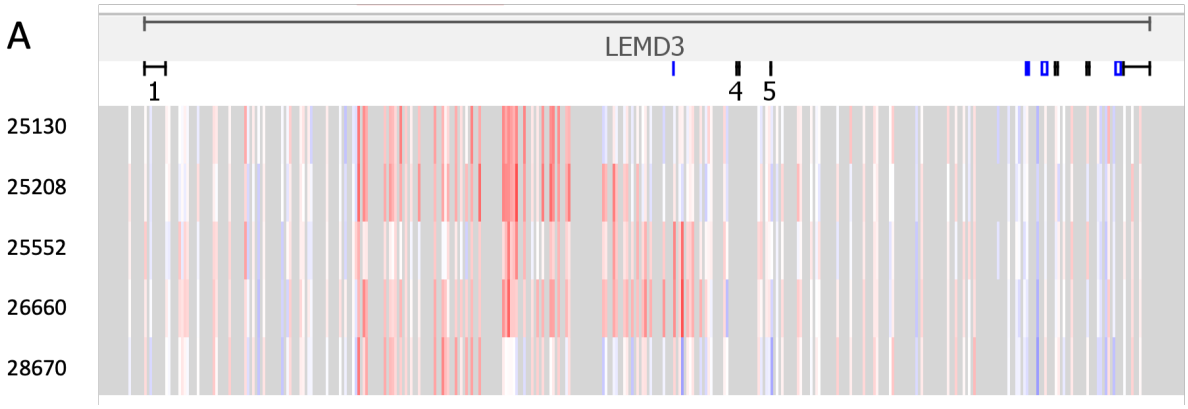
Supplementary figures



Supplementary figure S1. Patterns of gene deletions observed across full cohort of 78 SNP arrays. Combinations of deletions grouped by patterns observed. *CDKN2A/B/PAX5* combined deletion commonly represented del(9p).

A



B

Patient ID	Sex (M/F)	Age (yrs)	Genetic subgroup	WCC ($x10^9$/L)	Deleted segment	Size of deletion (bp)	Outcome
25130	F	62	*IGH-CRLF2*	33.6	chr12:65,579,942-65,597,922	17,980	Died after 1 month
25208	M	62	*BCR-ABL1*	205.4	chr12:65,579,942-65,602,114	22,172	Alive after 9 years
25552	M	61	*P2RY8-CRLF2*	2.9	chr12:65,579,801-65,611,980	32,179	Died after 4 months
26660	F	62	*BCR-ABL1*	18.2	chr12:65,579,942-65,608,678	28,736	Alive after 7 years
28670	F	61	*BCR-ABL1*	1.6	chr12:65,579,942-65,591,462	11,520	Died after 2 months

Supplementary figure S2. Focal *LEMD3* deletions. SNP array data shown with each bar representing a probe (A). Red colours indicate negative log2 ratio (copy number loss), blue colours represent positive log2 ratio (copy number gain), and white represents no copy number change. Demographic, clinical and genetic data (B) indicating that all affected patients had *BCR-ABL1* or *CRLF2* rearrangements.

Supplementary table S1. Targeted gene sequencing panel.

Gene	Region captured
ABL1	whole gene
ABL2	whole gene
ARID2	whole gene
ASXL1	exons
ATM	exons
CREBBP	exons
CSF1R	whole gene
DGKH	whole gene
DNMT3A	exons
ETV6	whole gene
FLT3	whole gene
FOXO1	exons
IKZF1	whole gene
IKZF2	exons
IKZF3	exons
IL7R	exons
JAK1	exons
JAK2	whole gene
JAK3	exons
KDM6A	whole gene
KMT2C	exons
KRAS	exons
MEF2C	whole gene
MEF2D	whole gene
NF1	whole gene
NOTCH1	exons
NR3C1	exons
NRAS	exons
NT5C2	exons
PAX5	whole gene
PDGFRB	whole gene
PTEN	whole gene
PTPN11	exons
RAG1	whole gene
RB1	exons
RUNX1	exons
SH2B3	exons
TCF3	whole gene
TCF4	whole gene
TET2	exons
TFDP3	exons
TOX	exons
TP53	exons
ZFHX3	exons

Supplementary table S2. Primary chromosomal abnormalities in 210 adults aged ≥60 years recruited to UKALL14 or UKALL60+.

Immunophenotype	Cytogenetics	Number of cases (%)	Percentage male	Median age (yrs)
BCP-ALL	***BCR-ABL1***	55 (26%)	40%	64
	TCF3-PBX1	3 (1%)	33%	64
	KMT2A-v	12 (6%)	33%	64
	HeH	2 (1%)	100%	64.5
	HoTr	29 (14%)	43%	64
	B-other	88 (42%)	60%	65
T-ALL		11 (5%)	64%	64
No data		10 (5%)	40%	63
Total		210 (100%)	50%	64

Supplementary table S3. Complete cohort of 210 adults aged ≥60 years with ALL included in study.

Patient ID	Sex	Age	Trial	% BM Blasts	SNP array	Genetic subgroup	Genetic risk group	Karyotyping +/- routine FISH	B-other FISH screening	SNP arrays	MLPA	Targeted NGS	Karyotype
24309	Male	63	UKALL14	80	Illumina	Complex	Very high risk	✓	✓	✓	✓		45~48,XY,t(2;18)(p11;q21),-4,-5,der(9)t(1;9)(q2;q2),del(13)(q12q14),del(14)(q1q2),add(16)(q1),i(17)(q10),+21,+1~3mar[cp11]
24813	Female	62	UKALL14	50	Illumina	No data	Standard risk			✓	✓	✓	NDS
24890	Male	65	UKALL14	100	Illumina	B-other	Standard risk	✓		✓	✓	✓	46,XY[10]
24919	Female	64	UKALL14	95	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		46,XX,t(9;22)(q34;q11)[8]/46,XX[2]
24983	Female	60	UKALL14	73	NA	BCR-ABL1	Tyrosine kinase activating	✓					52,XX,+2,+5,add(9)(p1),t(9;22)(q34;q11),+16,+21,+der(22)t(9;22),+mar[3]/52,XX,+2,+5,+5,der(9)add(9)(p1)t(9;22),+16,+21,+der(22)t(9;22), der(22)t(9;22)[5]/46,XX[2]
25082	Female	62	UKALL14	95	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓	✓	53,XX,+X,+2,+6,t(9;22)(q34;q11.2),+14,+18,+21,+der(22)t(9;22)[7]/54,idem,+der(22)t(9;22)[3]
25100	Female	63	UKALL14	79	Illumina	KMT2A-v	High risk	✓		✓		✓	46,XX,t(1;11)(p32;q23)[11]
25101	Female	63	UKALL14		NA	Complex	Very high risk	✓	✓				45,XX,-9,del(20)(q11.2q13?3),+mar1,+mar2,+mar3[cp3]/46,XX[22]
25102	Female	63	UKALL14	79	NA	HoTr	Very high risk	✓					38,X,-X,add(1)(p3),-3,-4,-5,-7,-9,add(9)(p1),add(10)(q24),-15,-17,-19,-20,-22,+3mar[cp14]/74~75,idemx2,-2,-6,inc[cp11]
25123	Male	60	UKALL14	92	NA	HoTr	Very high risk	✓					63~71<2n>,XY,+X,+X,+Y,+1,+1,+2,+4,+5,+del(5)(q?15q?33),+6,+6,+10,+10,+11,+11,+12,+12,+15,+18,+18,+19,+19,+22,+22[cp5]/46,XY[5]
25130	Female	62	UKALL14	100	Illumina	CRLF2-r	Very high risk	✓	✓	✓	✓	✓	46,XX[20]
25208	Male	62	UKALL14	66	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓	✓	46,XY,-9,t(9;22)(q34;q11),add(10)(q2?2),+der(22)t(9;22)(q34;q11)[2]
25235	Male	63	UKALL14	70	NA	ZNF384-r	Standard risk	✓	✓				FAILED
25237	Female	63	UKALL14	60	NA	No data	Standard risk				✓		46,XX[20]
25246	Male	64	UKALL14	42	Illumina	CRLF2-r	Very high risk	✓	✓	✓	✓		46,XY,der(19)t(1;19)(q12;p13.3)[2]/46,idem,t(5;18)(q33:q23)[8]/46,XY[10]
25247	Male	64	UKALL14	95	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓	✓	47,XY,t(9;22)(q34;q11),+10[10]
25267	Female	63	UKALL14	1	Illumina	MEF2D-r	Standard risk	✓	✓	✓	✓	✓	45~47,XX,+1,dic(1;17)(p32;q25),inc[cp3]
25293	Male	63	UKALL14	99	NA	B-other	Standard risk	✓					92,inc[2]/46,XY[18]
25344	Female	61	UKALL14	80	Illumina	B-other	Standard risk	✓	✓	✓	✓		FAILED
25346	Male	64	UKALL14	40	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓	✓	46,XY,t(9;22)(q34;q11)[9]
25371	Female	60	UKALL14	50	Illumina	CRLF2-r	Very high risk	✓	✓	✓	✓		46,XX[20]
25373	Male	65	UKALL14	32	Illumina	B-other	Standard risk	✓		✓	✓		46,XY,del(9)(q13q22)[4]/46,XY[14]
25415	Female	64	UKALL14		NA	B-other	Standard risk	✓	✓				46,XX[20]
25426	Female	64	UKALL14	8	NA	B-other	Standard risk	✓	✓				46,XX
25437	Female	64	UKALL14	88	Illumina	HoTr	Very high risk	✓		✓		✓	66~69<3n>,XXX,-1,-3,+der(1;3)(p10;q10)x2,+6,-7,-8,-9,+12,-13,-14,-15,-16,-17,+18,+21,+22,+mar1,+mar2[cp8]/46,XX[2]
25451	Male	63	UKALL14	88	Illumina	ZNF384-r	Standard risk	✓	✓	✓	✓	✓	46,XY[20]
25491	Male	63	UKALL14	92	NA	BCR-ABL1	Tyrosine kinase activating	✓					43,X,-Y,-7,-7,add(9)(p?2),t(9;22)(q34;q11),-10,-11,add(13)(q32),+2mar[cp7]/46,XY[2]
25548	Female	60	UKALL14	16	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		46,XX,t(9;22)(q34;q11)[10]
25552	Male	61	UKALL14	80	Illumina	CRLF2-r	Very high risk	✓		✓	✓	✓	46,XY[20]
25685	Male	62	UKALL14		NA	No data	Standard risk						46,XY[22]
25688	Male	62	UKALL14	82	NA	T-cell	Standard risk	✓					46,XY[23]
25694	Male	60	UKALL14	4	NA	KMT2A-v	High risk	✓					failed
25695	Male	63	UKALL14	80	NA	HoTr	Very high risk	✓					74~79<3n>,XXY,+Y,+1,?add(2)(p1),+add(2)(p1),-3,+4,+5,+6,+9,+add(11)(q2),-12,+14,-15,-15,-15,-16,+18,+19,+21,+21,+21,+1~3mar[cp6]
25709	Female	62	UKALL14	100	NA	KMT2A-v	High risk	✓			✓		46,XX,t(3;4;11)(p13;q21;q23)[10]
25793	Female	67	UKALL60	100	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓		✓	46,XX,der(9)t(9;22)(q34;q11)t(9;21)(q34;q22.3),der(21)t(9;22)t(9;21),der(22)t(9;22)[8]/46,XX[3]
25794	Female	65	UKALL60	89	NA	HoTr	Very high risk	✓					36,X,-X,-2,-3,-4,-7,-10,-13,-15,-16,?-17,inc[6]/?72,inc[5]/46,XX[2]
25842	Male	64	UKALL14		NA	HoTr	Very high risk	✓					37~39,XY,-2,-3,-4,-9,-13,-16,-17,-20[cp8]/60~62<3n>,XXY,+Y,-2,-3,-5,-9,-13,-14,-16,-17,-20[cp2]
25893	Female	78	UKALL60	92	Affymetrix	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		47,XX,+X,?add(3)(q21),i(9)(q10)t(9;22)(q34;q11)[5]/45,XX[5]
25894	Male	63	UKALL60	98	NA	IGH@-r	Standard risk	✓					44,XY,-8,-13,der(14)t(8;14)(q11;q32)[13]/44,idem,add(19)(p13.3)[4]/46,XY[3]
25895	Male	67	UKALL60	87	NA	B-other	Standard risk	✓	✓				46,XY[20]
25907	Male	70	UKALL60	96	NA	IGH@-r	Standard risk	✓	✓				47,XY,+X,?t(18;22)(q11;q21)[1]/46,XY[3]
25925	Female	61	UKALL14	86	NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XX,?t(3;14)(q24;q32),t(9;22)(q34;q11),-11,+mar[1]/47,idem,+der(22)t(9;22)[5]/46,XX[4]
25949	Female	61	UKALL14	90	NA	B-other	Standard risk	✓					FAIL
25953	Female	71	UKALL60	90	Affymetrix	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		46,XX[10]
25967	Male	60	UKALL14	95	Illumina	Complex	Very high risk	✓	✓	✓	✓	✓	46,XY,+5,-6,dic(7;9)(p13;p11),add(14)(q32),del(17)(p11),+21[18]/46,XY[2]
26062	Male	61	UKALL14	84	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		46,XY,t(9;22)(q34;q11)[5]/48~51,XY,+X,+6,+8,t(9;22)(q34;q11),+16,+der(22)t(9;22)[cp12]/46,XY[2]
26609	Male	83	UKALL60	50	Affymetrix	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		45,XY,-7,t(9;22;11)(q34;q11;q13)[19]/46,XY[1]
26610	Male	65	UKALL60	63	Affymetrix	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		46,XY,der(9)del(q)(p1)t(9;22)(q34;q11),der(22)t(9;22)(q34;q11)[13]/46,XY[17]
26611	Male	68	UKALL60	83	NA	B-other	Standard risk	✓	✓		✓		47,XY,+X,del(16)(?q1),i(17)(q10)[8]/46,XY[8]
26612	Male	66	UKALL60	3	NA	B-other	Standard risk	✓	✓				46,XY[10]
26613	Male	66	UKALL60	81	NA	Complex	Very high risk	✓					44~45,XY,del(3)(q?2q?2),-7,+8,del(9)(p2?1),-20[cp9]/46,XY[1]
26614	Male	75	UKALL60	98	Affymetrix	B-other	Standard risk	✓		✓	✓	✓	Failed
26621	Female	69	UKALL60	90	Affymetrix	T-cell	Standard risk	✓		✓	✓		FAIL
26659	Male	60	UKALL14	0	Illumina	HoTr	Very high risk	✓		✓			Fail

26660	Female	62	UKALL14	84	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓	✓	46,XX,t(9;22)(q34;q11.2)[8]/46,XX[37]
26682	Female	63	UKALL60	35	Affymetrix	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		44,XX,-7,der(9;12)(q10;q10),t(9;22)(q34;q11.2),-13,+mar[8]/46,XX[2]
26706	Male	60	UKALL14	89	Illumina	HoTr	Very high risk	✓		✓			39,XY,add(2)(p13),-3,-4,-7,-8,i(9)(q10),-12,-13,-16,-17,+2mar[cp3]
26726	Male	66	UKALL60	88	Affymetrix	HeH	Standard risk	✓		✓	✓		Not Done
26732	Female	64	UKALL14		NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XX[20]
26768	Female	70	UKALL60	89	NA	B-other	Standard risk	✓					46,XX,add(3)(q27)[19]/46,XX[1]
26971	Male	67	UKALL60	50	Affymetrix	B-other	Standard risk	✓	✓	✓	✓		46,XY,add(1)(q1)[5]/46,XY[5]
26990	Female	63	UKALL60	94	NA	B-other	Standard risk	✓	✓				46,XX[20]
26995	Male	70	UKALL60		Affymetrix	B-other	Standard risk	✓	✓	✓	✓		46,XY[20]
27026	Female	63	UKALL14		Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		67~73,XX,+X,t(9;22)(q34;q11),+ider(22)t(9;22)x2,inc[cp5]
27033	Male	72	UKALL60	72	NA	B-other	Standard risk	✓	✓				46,XY[20]
27043	Female	65	UKALL14	90	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		46,XX,t(2;9)(p21;p23),add(6)(q21),t(9;22)(q34;q11),add(21)(q21)[8]/46,XX[2]
27071	Female	60	UKALL14	90	Illumina	B-other	Standard risk	✓	✓	✓	✓		46,XX[20]
27085	Female	63	UKALL60	92	Affymetrix	BCR-ABL1	Tyrosine kinase activating	✓		✓			46,XX,t(9;22)(q34;q11.2),der(19)t(8;19)(q13;p13.3)[8]/46,XX[2]
27121	Female	64	UKALL60		NA	HoTr	Very high risk	✓			✓		36,X,-X,-2,-3,-4,-7,-12,-13,-15,-16,-17[7]/46,XX[3]
27147	Female	69	UKALL60	86	NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XX,t(9;22)(q34;q11)[3]
27181	Male	65	UKALL14	40	Illumina	IGH@-r	Standard risk	✓	✓	✓	✓	✓	46,XY,inv(14)(q11q32)[2]/46,XY[18]
27219	Female	65	UKALL60	90	NA	B-other	Standard risk	✓	✓				Failed
27298	Male	66	UKALL60	90	Affymetrix	B-other	Standard risk	✓	✓	✓	✓		46,XY[20]
27333	Female	63	UKALL14	73	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		46,XX,t(9;22)(q34;q11.2)[13]/47,XX,der(9)t(9;22)(q34;q11.2)add(9)(p13),der(22)t(9;22)(q34;q11.2),+der(22)t(9;22)[3]/46,XX[4]
27389	Female	73	UKALL60		Illumina	KMT2A-v	High risk	✓		✓		✓	47,XXX,t(11;19)(q23;p13)[7]/46,XX[3]
27391	Male	65	UKALL60		Affymetrix	B-other	Standard risk	✓		✓	✓		46,XY[7]
27392	Female	73	UKALL60	72	Affymetrix	HoTr	Very high risk	✓		✓	✓		46,XX[20]
27395	Male	60	UKALL14	98	NA	T-cell	Standard risk	✓					47,XY,+19,inc[4]
27407	Female	69	UKALL60	61	NA	HoTr	Very high risk	✓					64~70<3n>,XX,-X,+1,+2,+2,-3,-4,+5,+6,-7,-9,+10,+11,-13,-13,-15,-16,-17,-18,-19,?der(19)t(13;19)(q1;q13),-20,+21,+3~7mar[cp6]
27408	Male	70	UKALL60	0	NA	T-cell	Standard risk	✓					46,XY,t(7;14)(p15;q23)[5]/46,XY[2]
27409	Male	74	UKALL60	8	NA	B-other	Standard risk	✓					Failed
27441	Female	61	UKALL14	90	Illumina	No data	Standard risk			✓	✓		NDS
27452	Male	62	UKALL14	40	NA	B-other	Standard risk	✓	✓				46,XY,i(9)(q10)[10]
27490	Male	64	UKALL60	40	Affymetrix	B-other	Standard risk	✓	✓	✓			~92,inc[11]/46,XY[2]
27508	Male	61	UKALL14	92	NA	HoTr	Very high risk	✓					64~66<3n>,XX,-Y,-3,-7,+12,+13,-15,-16,+21[cp3]/80~86<4n>,X,-X,-Y,-Y,-3,-4,-5,-6,-7,-7,-9,-10,+12,+13,-15,-16,+17,-19,-20,-22[cp6]/45,X,-Y[1]
27509	Male	69	UKALL60	60	Affymetrix	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		45,XY,der(7;9)(q10;q10)t(9;22)(q34;q11.2),der(22)t(9;22)(q34;q11.2)[11]
27537	Female	67	UKALL60	87	Affymetrix	HoTr	Very high risk	✓		✓	✓		69,XX,+1,+1,+2,+4,+4,+5,+6,+6,+8,+10,+10,+11,+11,+12,+14,+14,+18,+18,+19,+21,+21,+22,+mar[3]/46,XX[5]
27554	Female	78	UKALL60	75	Affymetrix	B-other	Standard risk	✓	✓	✓	✓		46,XX,add(12)(q13)[3]/46,XX[27]
27555	Male	64	UKALL60	0	Affymetrix	HoTr	Very high risk	✓		✓	✓		67<2n>,XY,+X,+Y,+1,+1,+2,+4,+5,+6,+?del(6)(q?25),+8,?add(9)(p21),+10,+11,+11,+12,+14,+18,+19,+21,+21,+22,+22,inc[1]/46,XY[10]
27556	Female	75	UKALL60	50	NA	B-other	Standard risk	✓	✓				46,XX[9]
27557	Male	61	UKALL14	21	NA	T-cell	Standard risk	✓					46,XY[20]
27579	Female	60	UKALL60	55	NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XX,t(2;9;22)(p21;q34;q11.2)[6]/46,XX[4]
27583	Female	61	UKALL60	95	Affymetrix	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		51,XX,+X,+4,t(9;22)(q34;q11.2),+14,+17,+der(22)t(9;22)[10]
27584	Female	76	UKALL60	90	Affymetrix	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		46,XX,t(9;22)(q34;q11)[7]/45,idem,-7[3]/46,XX[1]
27585	Female	66	UKALL60	62	Affymetrix	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		46,XX,t(9;22)(q34;q11)[11]
27596	Male	62	UKALL60	64	Affymetrix	HoTr	Very high risk	✓		✓	✓		38~39,XY,-3,-4,-5,-7,-9,-15,-16,inc[cp4]/46,XY[16]
27640	Male	67	UKALL60	97	NA	B-other	Standard risk	✓	✓				45,XY,dic(7;9)(p1?1;p1?1)/46,XY[12]
27642	Female	72	UKALL60	90	Affymetrix	T-cell	Standard risk	✓		✓	✓	✓	Failed
27668	Male	68	UKALL60	60	NA	BCR-ABL1	Tyrosine kinase activating	✓					Fail
27752	Female	73	UKALL60	48	Affymetrix	B-other	Standard risk	✓	✓	✓	✓		46,XX[20]
27754	Female	63	UKALL14		Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		Fail
27810	Female	79	UKALL60	90	NA	No data	Standard risk						NDS
27811	Male	64	UKALL14		NA	HoTr	Very high risk	✓					63~65,XY,+X,+Y,+1,+4,+5,+6,+8,+10,+11,+12,+18,+18,+19,+21,+21,+22,+22,+1~5mar[cp9]/46,XY[1]
27812	Male	65	UKALL14	99	Illumina	TCF3-PBX1	Standard risk	✓		✓	✓		46,XY,der(19)t(1;19)(q23;p13)[10]/46,XY[2]
27819	Female	65	UKALL60	90	Affymetrix	B-other	Standard risk	✓	✓	✓	✓		46,XX[20]
27833	Female	73	UKALL60	98	Affymetrix	IGH@-r	Standard risk	✓	✓	✓	✓	✓	Failed
27836	Male	63	UKALL14	61	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		45,XX,-7,t(9;22)(q34;q11.2),t(12;21)(p13;q22)[5]/46,XY,idem,+der(22)t(9;22)(q34;q11.2)[5]
27887	Female	68	UKALL60	80	NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XX,t(9;22)(q34;q22)[8]/46,XX[2]
27919	Female	82	UKALL60	11	NA	B-other	Standard risk	✓					Fail
27930	Male	60	UKALL60	82	NA	B-other	Standard risk	✓					46,XY[20]
27978	Male	66	UKALL60	30	NA	No data	Standard risk	✓					No sample
28011	Male	61	UKALL14		Illumina	CRLF2-r	Very high risk	✓	✓	✓	✓		46,XY,-2,add(7)(q3),add(12)(p11),+mar[3]/46,XY[19]
28032	Female	69	UKALL60	98	NA	T-cell	Standard risk	✓					47,XX,+19[7]/46,XX[3]. ish der(8)(IGHx1), 14(IGHx1)

28033	Female	63	UKALL60	92	NA	KMT2A-v	High risk	✓					46,XX,t(4;11)(q21;q23),inc[5]
28034	Male	74	UKALL60	4	NA	No data	Standard risk						Not analysed
28039	Male	76	UKALL60	88	NA	CRLF2-r	Very high risk	✓	✓		✓		45,XY,-7,-15,-17,+mar[10]/46,XY[1]
28050	Male	66	UKALL60	98	NA	B-other	Standard risk	✓	✓				Fail
28051	Male	66	UKALL60	28	NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XY,t(9;22)(q34;q11)[3]/46,XY[5]
28057	Female	64	UKALL14		Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓	✓	46,XX,t(9;22)(q34;q11),inc[3]/46,XX,inc[2]
28076	Male	63	UKALL60	80	NA	B-other	Standard risk	✓					46,XY[20]
28091	Female	64	UKALL14	76	NA	T-cell	Standard risk	✓					Failed
28092	Female	71	UKALL60	80	NA	HoTr	Very high risk	✓					37,XX,del(2)(q21)(q31),-3,-4,-5,-7,-9,-13,-16,-17,-20[7]/46,XX[3]
28093	Male	72	UKALL60		NA	B-other	Standard risk	✓					Fail
28104	Female	64	UKALL60		NA	TCF3-PBX1	Standard risk	✓					46,XY[20]
28105	Female	78	UKALL60	90	NA	B-other	Standard risk	✓					46,XX,del(12)(p?13)[3]/46,XX[7]
28135	Female	79	UKALL60	75	NA	BCR-ABL1	Tyrosine kinase activating	✓					45,XX,-7,t(9;22)(q34;q11)[10]
28149	Female	64	UKALL14	80	Illumina	B-other	Standard risk	✓		✓	✓		46,XX,dic(9;12)(p13;p12)[5]/46,XX[5]
28150	Male	65	UKALL60	95	NA	BCR-ABL1	Tyrosine kinase activating	✓					45,XY,add(3)(p21),add(6)(q21),-7,-9,-21,add(22)(q11),+2mar,inc[cp6]/46,XY[14]
28168	Male	65	UKALL14		Illumina	B-other	Standard risk	✓	✓	✓	✓		45,XY,inv(2)(p1?5q1?3),dic(9;12)(p13;p13)[10]/46,XY[1]
28182	Female	60	UKALL14	90	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓	✓	46,XX,t(9;22)(q34.1;q11)[2]/46,idem,der(5)t(1;5)(q23;q21)[7]/46,XX[1]
28194	Male	66	UKALL60		NA	B-other	Standard risk	✓	✓				Failed
28196	Male	61	UKALL14	99	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		46,XY,add(9)(q34),der(17)t(17;22)(q21;q11),der(22)t(9;22)(q34;q11)[4]/46,XY,add(4)(q31),add(5)(q31),add(9)(q34),der(17)t(7;22)(q21;q11),der(22)t(9;22)(q34;q11)[6]
28235	Female	65	UKALL60	90	NA	CRLF2-r	Very high risk	✓	✓				46,XX,der(19)t(1;19)(q12;q13)[4]/46,XX[6]
28310	Female	66	UKALL60	36	NA	B-other	Standard risk	✓	✓				45~46,XX,add(9)(p13)[4]/45~46,sl,del(13)(q1?3q3?2)[3]/44~45,sdl1,i(17)(q10)[cp2]/46,XX[9]
28312	Female	67	UKALL60	94	NA	BCR-ABL1	Tyrosine kinase activating	✓					45,XX,t(9;22)(q34;q11.2),add(9)(p?21),-11,der(12)t(11;12)(q23;p13)[7]/46,XX[1]
28317	Male	80	UKALL60	72	NA	B-other	Standard risk	✓	✓				46,XY[20]
28334	Male	64	UKALL14	27	NA	HoTr	Very high risk	✓					39,XY,del(3)(q1?2),-4,-10,-13,-15,-17,-18,-20,-22,+mar[1]/67~69<4n>,XXYY,-2,-2,del(3q)x2,-4,-4,-5,-6,-7,-7,-9,-10,-11,-12,-13,-13,-14,-14,-15,-15,-17,-18,-19,-19,+1~5mar[cp4]/46,XY[5]
28335	Male	63	UKALL14		Illumina	B-other	Standard risk	✓		✓	✓	✓	Failed
28350	Female	62	UKALL14	72	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓	✓	45,XX,-7,ins(9;?)(q13;?),t(9;22)(q34;q11.2)[9]/46,XX[6]
28361	Male	67	UKALL60	70	NA	HoTr	Very high risk	✓					36<2n>,XY,del(2)(q33q37),-3,-4,-5,-7,-9,-13,-15,-16,-17,-20[6]/46,XY[4]
28370	Male	81	UKALL60		NA	KMT2A-v	High risk	✓					45,X,-Y,t(11;19)(q23;p13.3)[9]/45,X,-Y[5]
28403	Male	71	UKALL60	92	NA	KMT2A-v	High risk	✓					47,XY,+X,t(4;11)(q21;q23)[3]/47,idem,del(17)(p11.2)[5]/47,idem,add(17)(p11.2)[2]
28404	Female	63	UKALL60	77	NA	HoTr	Very high risk	✓					66~68<3n>X,-X,-X,+1,-2,-3,-4,+5,+6,-7,+8,-9,+10,-12,-15,-16,-17,+18,+21,+21,+22,inc[cp8]/46,XX[2]
28406	Male	74	UKALL60	81	NA	HoTr	Very high risk	✓					65~67,XX,-Y,+2[2],-3[4],-4,-5,+6,-7,+8[4],-9,+10,+11[4],-13[3],-14,-15,der(16)t(11;16)(q1?2;p12)[3],-17,+19[4],-20,+21,+22[cp5]/64~65,XX,-Y,-3,-4,-5,+6,-7,+8,-9,+10,+11,-13,-14,-15,-16,der(16)t(11;16)(q1?2;p12)[3],-17,+19,-20,+21,+22[cp4]/44,X,-Y,der(13;14)(q10;q10)?c[10]/45,XY,der(13;14)(q10;q10)?c[1]
28456	Male	62	UKALL14	100	NA	B-other	Standard risk	✓					Failed
28581	Female	65	UKALL14	88	Illumina	KMT2A-v	High risk	✓		✓	✓	✓	47,XX,t(4;11)(q21;q23),+6[11]
28620	Male	60	UKALL14	91	NA	BCR-ABL1	Tyrosine kinase activating	✓					Failed
28644	Female	64	UKALL14	95	Illumina	HoTr	Very high risk	✓		✓			37<2n>,XX,-3,-4,-5,-7,-9,add(14)(q32),-15,-16,-17,-20[5]/68<3n>,XX,-X,-4,-5,-6,-7,+8,-9,+14,-15,-17,+18,+19,+21,+22,+mar[cp3]/46,XX[5]
28670	Female	61	UKALL14	94	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓	✓	45,XX,t(2;7)(p1;p1),der(3)t(3;5)(q13;q15),-5,der(9)add(9)(p1)t(9;22)(q34;q11),add(11)(q15),add(12)(p1),der(22)t(9;22)(q34;q11)[4]/46,XX[6]
28905	Male	60	UKALL14	85	NA	B-other	Standard risk	✓	✓				46,XY[20]
28934	Female	60	UKALL14	90	Illumina	KMT2A-v	High risk	✓		✓	✓		46,XX,der(4)t(4;11)(q21;q23)ins(4;13)(q21;q1?q34),der(11)t(4;11)
28945	Female	64	UKALL14	89	NA	B-other	Standard risk	✓	✓				45,X,-X,add(9)(p2)[10]
29089	Female	60	UKALL14	90	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		46,XX,t(9;22)(q34;q11.2)[9]/46,XX[1]
29202	Male	61	UKALL14	99	NA	B-other	Standard risk	✓					45,XY,del(4)(q21q25),der(9)add(9)(p13)add(9)(q22),-16[10]
29407	Female	60	UKALL14	94	Illumina	HoTr	Very high risk	✓		✓		✓	31~35,X,-X,-2,dic(8;13)(q10;q10),+19,-20[cp3]/57~67,XX,+1,+1,+2,+4,+6,+6,dic(8;13)(q10;q10)x2,+10,+11,+11,+i(11)(q10),+12,+14,+14,+18,+18,+19,+19,+21,+21,+22,+22,+1~6mar[cp11]/46,XX[1]
29453	Male	63	UKALL14	60	NA	T-cell	Standard risk	✓					NDS
29454	Female	65	UKALL14	90	NA	B-other	Standard risk	✓					46,XX,del(9)(q13q22)[6]/46,XX[4]
29481	Female	69	UKALL60	7	NA	B-other	Standard risk	✓					46,XX[20]
29517	Male	65	UKALL14	92	NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XY,t(9;22)(q34;q11.2),add(21)(p11)[5]/46,XY[5]
29519	Female	61	UKALL14	86	NA	B-other	Standard risk	✓					82~84,XXXX,+X,-3,-7,-7,-8,-9,-9,+12,-15,-15,-16,-17,-18,-20,-20,+21,+21[cp10]
29589	Male	61	UKALL14	82	Illumina	BCR-ABL1	Tyrosine kinase activating	✓		✓	✓		47,XY,+2,t(9;22)(q34;q11.2)[4]/48,XY,+2,t(9;22)(q34;q11.2),+der(22)t(9;22)(q34;q11.2)[9]/46,XY[7]
29655	Female	65	UKALL60	60	NA	BCR-ABL1	Tyrosine kinase activating	✓					Not reported
29710	Male	67	UKALL60	93	NA	B-other	Standard risk	✓	✓				49,XY,+8,+2mar[6]/46,XY[4]
29741	Male	77	UKALL60	77	NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XY,t(9;22)(q34;q11.2)[1]/46,XY[12]
29808	Male	66	UKALL60	96	NA	IGH@-r	Standard risk	✓					46,XY,add(2)(q?37),add(8)(q13),add(14)(q32)[10]/46,XY[7]
29809	Male	63	UKALL60	64	NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XX,t(9;22)(q34;q11.2)[5]/46,XX[5]
29848	Female	68	UKALL60	13	NA	B-other	Standard risk	✓					Failed

29849	Female	70	UKALL60	79	NA	HoTr	Very high risk	✓					39~40,XX-3,-4,-7,-9,-17,-20,?add(20)(q13.3),-22,i(22)(q10),+mar[cp7]/73~76<3n>XXX,+X,+1,-3,-4,+6,-7,+8,-9,+10,+12,+13,+14-17,?add(20)(q13.3),-22,i(22)(q10),+2~4mar[cp3]/109~110<5n>,XXXXX,+X,-3,-4,-4,-5,+6,+6,-7,-7,+8,-9,+10,-17,-17,-20,?add(20)(q13.3),?add(20)(q13.3),-22,-22,-22,i(22)(q10),i(22)(q10),+2~3mar[cp3]/46,XX[7]
29881	Male	63	UKALL60	90	NA	BCR-ABL1	Tyrosine kinase activating	✓					Not done
29882	Female	71	UKALL60	70	NA	HoTr	Very high risk	✓					63~67,XX,+X,+1,+1,+2,+4,+4,+6,+7,+8,+8,+10,+10,+11,+11,+12,+12,+14,+14,+21,+21,+22,+22[cp6]/46,XX[4]
29908	Female	62	UKALL14		Illumina	KMT2A-v	High risk	✓		✓		✓	46,XX,t(4;11)(q21;q23),inc[2]/46,XX[1]
29958	Male	79	UKALL60	45	NA	BCR-ABL1	Tyrosine kinase activating	✓					Not Done
30031	Female	73	UKALL60	90	NA	BCR-ABL1	Tyrosine kinase activating	✓					50,XX,+2,del(9)(p13p22),t(9;22)(q34;q11),+11,+21,+der(22)t(9;22)(q34;q11)[8]/46,XX[2]
30063	Male	69	UKALL60	85	NA	No data	Standard risk						Failed. arr(1-22XY)cx, (7)x1, (17)x1
30066	Male	63	UKALL14		NA	HeH	Standard risk	✓					47,XY,+8[4]/52,XY,+6,+7,+8,+12,+17,+22[6]
30085	Male	67	UKALL60	68	NA	ZNF384-r	Standard risk	✓	✓				46,XY[20]
30086	Female	69	UKALL60	90	NA	B-other	Standard risk	✓	✓				46,XX[?]
30102	Female	67	UKALL60	95	NA	CRLF2-r	Very high risk	✓	✓				46,XX,del(9)(p1p2)[9]/46,XX[1]
30103	Female	64	UKALL14		NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XX,t(9;22)(q34;q11.2)[1]/46,idem,add(6)(q27),del(9)(p13)[4]/46,XX[3]
30175	Female	63	UKALL14		NA	B-other	Standard risk	✓					46,XX[16]
30236	Male	73	UKALL60	55	NA	T-cell	Standard risk	✓					45,XY,add(17)(p11.2)[3]/46,XY[17]
30237	Female	74	UKALL60	93	NA	B-other	Standard risk	✓					Failed. arr(1-22,X)x2
30297	Female	64	UKALL60	74	NA	CRLF2-r	Very high risk	✓	✓				46,XX,t(X;9)(p22;p13),der(15)t(1;15)(q21;p13)[cp8]/46,XX[4]
30298	Female	69	UKALL60	90	NA	B-other	Standard risk	✓					46,XX,der(7)ins(7;?)(q22;?)[7]/46,XX[3]
30299	Female	74	UKALL60		NA	CRLF2-r	Very high risk	✓	✓				Not reported
30300	Female	74	UKALL60	95	NA	KMT2A-v	High risk	✓					46,XX,t(4;11)(q21;23)[10]
30315	Female	69	UKALL60	83	NA	HoTr	Very high risk	✓					33~38,XX,-3,-7,-8,-13,-14,-15,-18[cp4]/46,XX[9]
30331	Female	77	UKALL60	92	NA	HoTr	Very high risk	✓					36~37,X,-X,-3,-4,-5,-7,-9,-13,-16,-17,-20,-21,+1~2mar[cp5]
30334	Male	60	UKALL14		NA	B-other	Standard risk	✓					46,XY[20]
30347	Male	70	UKALL60	50	NA	B-other	Standard risk	✓					46,XY[20]
30378	Male	71	UKALL60	43	NA	B-other	Standard risk	✓	✓				Fail
30389	Female	83	UKALL60	85	NA	B-other	Standard risk	✓					92<4n>,XXXX,-3,+12,+12,-17[3]/46,XX[7]
30390	Male	73	UKALL60	71	NA	HoTr	Very high risk	✓					70<3n>,XYY,+1,-3,-4,+5,+6,-7,+8,+11,-12,-13,+14,-15,-16,-17,+18,+20,+21[2]/46,XY[6]
30402	Female	62	UKALL60	90	NA	TCF3-PBX1	Standard risk	✓					46,XX,del(6)(q16q21)[4]/46,idem,der(19)t(1;19)(q23;p13.3)[4]/46,XX[2]
30403	Male	71	UKALL60		NA	B-other	Standard risk	✓					46,XY[20]
30419	Female	64	UKALL60		NA	B-other	Standard risk	✓					46,XX[12]
30426	Male	72	UKALL60		NA	B-other	Standard risk	✓					46,XY[5]
30428	Female	61	UKALL14		NA	HoTr	Very high risk	✓					60,XX,+1,+1,+4,+6,+8,+8,+11,+13,+18,+19,+21,+21+22,+22,inc[cp3]/46,XX[7]
30438	Male	81	UKALL60	91	NA	Complex	Very high risk	✓	✓				45,XY,add(1)(q3),add(2)(p1),-6,-7,add(9)(p2),add(11)(q21),add(12)(p13),del(13)(q12q14),add(16)(p13),+mar[10]
30476	Male	71	UKALL60	59	NA	B-other	Standard risk	✓					Failed
30487	Male	60	UKALL14		NA	IGH@-r	Standard risk	✓					47,XY,+X,t(14;19)(q32;q13)[8]/46,XY[2]
30521	Male	66	UKALL60	79	NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XY,t(9;22)(q34;q11)[10]/46,XY[2]
30556	Male	75	UKALL60	95	NA	B-other	Standard risk	✓					47,XY,+5[2]
30557	Female	78	UKALL60	94	NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XX,+1,t(9;22)(q34;q11.2),der(16)t(1;16)(q11;q11)[13]/46,XX[1]
30623	Male	64	UKALL14		NA	KMT2A-v	High risk	✓					46,XY,der(4)(?11qter->11q23::4p1?4->4q21::11q23->11qter),der(11)t(4;11)(q21;q23),add(15)(q2?2)[12]
30641	Male	62	UKALL60	85	NA	B-other	Standard risk	✓					46,XY,?del(9)(p21p21)[4]/46,XY[16]
30721	Female	61	UKALL14		NA	No data	Standard risk						54,+X,+X,+6,+6,+11,+11,der(11;21)(p10;q10)x2,+22,+22[8]/46,XX[2]
31085	Female	62	UKALL14		NA	No data	Standard risk						67<3n>,XX,-X,-1,-5,+6,-7,+8,-9,+12,-13,-15,-16,+19,+21,+21,+1~2mar[cp8]/46,XX[4]
31095	Male	64	UKALL14		NA	T-cell	Standard risk	✓					Fail
31145	Male	62	UKALL14		NA	BCR-ABL1	Tyrosine kinase activating	✓					46,XY,t(9;22)(q34;q11.2)[2]/44,XY,-7,der(9)t(7;9)(p13;p22)t(9;22),der(13)t(7;13)(q32;q14),-18,der(22)t(9;22)[7]/46,XY[1]

Supplementary table S4. Demographic and genetic details of patients analysed by SNP array.

	SNP array cohort (n=78)	Complete cohort (n=210)	p-value
Demographics			
Median age (range)	64 (60-83)	64 (60-83)	
Female	58% (45)	50% (105)	0.29
Male	42% (33)	50% (105)	0.29
Genetic subgroups			
BCR-ABL1	40% (31)	26% (55)	0.03
HoTr	12% (9)	13% (28)	0.84
KMT2A fusion	6% (5)	6% (12)	0.78
TCF3-PBX1	1% (1)	1% (3)	1
HeH	1% (1)	1% (3)	1
B-other	36% (28)	42% (88)	0.42
T-ALL	1% (1)	5% (11)	0.19
Unknown	3% (2)	5% (10)	0.52

Supplementary table S5: Frequency of recurrent arm-level CNAs in cases lacking primary ploidy shift (n=68)

Abnormality	% of cases (n=68)	Subgroups represented (n)
del(9p)	22% (15)	*BCR-ABL1* (11), B-other (4)
gain of Ph*	12% (8)	*BCR-ABL1* (8)
gain 1q	10% (7)	B-other (4), *BCR-ABL1* (2), *TCF3-PBX1* (1)
-7	10% (7)	*BCR-ABL1* (5), B-other (2)
del(7p)	9% (6)	*BCR-ABL1* (4), B-other (2)
gain 21q	7% (5)	*BCR-ABL1* (2), B-other (3)
del(17p)	7% (5)	B-other (4), *BCR-ABL1* (1)
del(12p)	6% (4)	B-other (2), *BCR-ABL1* (1), T-ALL (1)
gain 14q	4% (3)	*BCR-ABL1* (3)
-9	4% (3)	*BCR-ABL1* (3)
+5	3% (2)	B-other (1), *BCR-ABL1* (1)
+2	3% (2)	*BCR-ABL1* (2)
+6	3% (2)	*BCR-ABL1* (1), *KMT2A-v* (1)
gain 8q	3% (2)	*BCR-ABL1* (1), B-other (1)
+11	3% (2)	B-other (1), *BCR-ABL1* (1)
del(13q)	3% (2)	*BCR-ABL1* (2)

Supplementary table S6. Characteristics of all *IKZF1* deletions

Patient	*IKZF1* deletion	Genetic subgroup
28670	ex.2-7	*BCR-ABL1*
25208	ex.2-7 and 2-8	*BCR-ABL1*
27026	ex.4-7	*BCR-ABL1*
26610	ex.4-7	*BCR-ABL1*
27043	ex.4-7	*BCR-ABL1*
29589	ex.2-7	*BCR-ABL1*
25247	ex.4-7	*BCR-ABL1*
25548	ex.4-7	*BCR-ABL1*
26660	ex.4-8	*BCR-ABL1*
27085	ex.2-7	*BCR-ABL1*
27754	ex.4-7	*BCR-ABL1*
28057	ex.4-7	*BCR-ABL1*
28182	ex.4-7	*BCR-ABL1*
24890	ex.4-7	B-other
25371	ex.2-7	*CRLF2-r*
25552	ex.4-7	*CRLF2-r*
25130	ex.2-8	*CRLF2-r*
25246	ex.4-8	*CRLF2-r*
28011	ex.4-7	*CRLF2-r*
28350	del(7p)/-7	*BCR-ABL1*
25953	del(7p)/-7	*BCR-ABL1*
26609	del(7p)/-7	*BCR-ABL1*
26682	del(7p)/-7	*BCR-ABL1*
27836	del(7p)/-7	*BCR-ABL1*
25344	del(7p)/-7	B-other
27298	del(7p)/-7	B-other
26706	del(7p)/-7	HoTr
28644	del(7p)/-7	HoTr
29407	del(7p)/-7	HoTr
27392	del(7p)/-7	HoTr
27596	del(7p)/-7	HoTr
25437	del(7p)/-7	HoTr
27555	del(7p)/-7	HoTr
26659	del(7p)/-7	HoTr
27537	del(7p)/-7	HoTr
27333	del(7p)/-7	*BCR-ABL1*
25793	del(7p)/-7	*BCR-ABL1*
27585	del(7p)/-7	*BCR-ABL1*
25967	del(7p)/-7	Complex
26614	del(7p)/-7	B-other

Supplementary table S7. Genomic details of *LEMD3* and *IKZF1* deletions

Gene	Patient ID	Deleted segment	Size of deletion (bp)	Deletion type	Deleted exons
LEMD3	25208	chr12:65,579,942-65,602,114	22172	Heterozygous	None
LEMD3	25130	chr12:65,579,942-65,597,922	17980	Heterozygous	None
LEMD3	28670	chr12:65,579,942-65,591,462	11520	Heterozygous	None
LEMD3	26660	chr12:65,579,942-65,608,678	28736	Heterozygous	ex. 2
LEMD3	25552	chr12:65,579,801-65,611,980	32179	Heterozygous	ex. 2-3
KDM6A	28011	chrX:44,810,083-44,867,059	56967	Hemizygous	ex. 3-4
KDM6A	29407	chrX:44,778,209-44,905,069	126860	Homozygous	ex. 3-8
KDM6A	25437	chrX:44,775,342-44,885,557	110215	Homozygous	ex. 3-6
KDM6A	27642	chrX:44,860,967-45,176,870	315903	Heterozygous	ex. 5-29

Supplementary table S8. Outcome of UKALL14 patients >60 years according to UKALL14 genetic risk categories. High risk patients were those with KMT2A fusions; Very high risk were those with complex karyotype, low hypodiplopidy/near triploidy, or CRLF2 rearrangement; TKA fusion patients were all BCR-ABL+; Standard risk patients were all other BCP-ALL patients

	Total	**Standard Risk**	**High Risk**	**Very High Risk**	***BCR-ABL1*+**	**T-Cell**
Total	95 (100)	33 (35)	7 (7)	21 (22)	28 (29)	6 (6)
White Cell Count						
<30	69 (73)	29 (88)	1 (14)	19 (90)	15 (54)	5 (83)
30-100	16 (17)	3 (9)	2 (29)	2 (10)	9 (32)	0 (0)
>100	10 (11)	1 (3)	4 (57)	0 (0)	4 (14)	1 (17)
Complete Remission						
Yes	70 (76)	27 (84)	5 (71)	12 (63)	21 (75)	5 (83)
No	22 (24)	5 (16)	2 (29)	7 (37)	7 (25)	1 (17)
Did not start treatment	3	1	0	2	0	0
5yr Survival Rates						
OS	24% (15-35)	41% (22-59)	0%	0%	24% (10-42)	0%
EFS	17% (9-27)	28% (12-47)	0%	0%	15% (4-33)	0%

Supplementary table S9. Patient outcomes according to type of *IKZF1* deletion

	Total	*IKZF1* ex.4-7 deletion	Other *IKZF1* deletions
Total	40 (100)	11 (28)	29 (73)
3-year survival rates			
Overall	19% (7-35)	10% (1-36)	24% (7-45)
Event-Free	11% (3-26)	0%	18% (4-38)
Relapse Rate	52% (26-83)	100%	28% (10-64)
Hazard Ratio			
Overall	-	1.37 (0.58-3.23), 0.467	1
Event-Free	-	1.56 (0.68-3.58), 0.298	1
Relapse Rate	-	2.46 (0.49-12.36), 0.275	1