Supplemental Material

Clinical implications and dynamics of Clonal Hematopoiesis in Anti-CD19 CAR T-Cell treated patients

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Supplemental Methods

Bioinformatic analysis

Paired-end reads (148bp+17bp+8bp+148bp) were sequenced on an Illumina NovaSeq 6000 and processed using our in-house Snakemake(1) pipeline. UMIs were extracted and FASTQs were generated using picard ExtractIlluminaBarcodes, IlluminaBasecallsToSam and SamToFastq subsequently.(2) Raw reads were aligned to GRCh38(3) using bwa mem(4) and UMI information was added using picard MergeBamAlignment.(2) Consensus reads were generated using fgbio GroupReadsByUmi with -s adjacency and fgbio CallMolecularConsensusReads with -M 3.(5) Consensus reads were aligned to GRCh38 using bwa mem and picard MergeBamAlignment. Fgbio FilterConsensusReadsQuality with a minimum of 3 consensus reads and default parameters was used for quality filtering of aligned consensus reads. Local realignment was performed using GATK3(6) RealignerTargetCreator and IndelRealigner.(7) Variants were called using VarDict(8) in single-mode with a minimum allele frequency of 0.0001. Variant calls were annotated using annovar(9) with following databases: refGen, cytoBand, clinvar_20200316, dbnsfp35c, gnomad30_genome, avsnp150, cosmic92_coding, cosmic92_noncoding, revel, nci60.

Filtering of somatic variants

The list of variants called by the above variant calling pipeline was further processed using an R-based filtering script with the following exclusion criteria:

1. Functional criteria
    a. synonymous variants
    b. intronic variants
2. Quality Criteria
    a. Strandbalance = 1
    b. Strandbalance = 0
3. Read count criteria
    a. Coverage < 50
    b. Variant supporting reads < 10
    c. Variant allele frequency < 0.01
4. Cohort/Population-based frequency criteria
    a. Allele frequency in the general population > 10% according to the gnomad30_genome database
    b. Variant frequency in this cohort > 20%
5. Germline/SNP Criteria
    a. 0.45 < VAF < 0.55 or VAF > 0.95 and allele frequency > 0.1% in the gnomad30_genome database or reported in the dbSNP database. Truncating variants at 0.45 < VAF < 0.55 were rescued, if not reported in the gnomad30_genome database and not reported in the dbSNP

Here, Strandbalance is defined as the ratio of variant reads on plus strand to minus strand. Hotspot variants such as *DNMT3A* R882C/H*, GNB1* K57E*, JAK2* V617F*, SF3B1* K666N and K700E, *SFRS2* P95L, *U2AF1* S34F, and Q157P/R were rescued. Variants passing these filters were manually evaluated in the Integrative Genome Viewer (Broad Institute, Cambridge, USA).

Supplemental References

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Supplemental Tables

Supplemental Table 1. List of genes covered by the custom sequencing panel (Twist Bioscience).

No.	Gene	Region	No.	Gene	Region	No.	Gene	Region
1	*DNMT3A*	Full	**16**	*RAD21*	Full	**31**	*ETV6*	Full
2	*TET2*	Full	**17**	*STAG2*	Full	**32**	*FLT3*	Full
3	*JAK2*	Full	**18**	*CHEK2*	Full	**33**	*GATA1*	Full
4	*ASXL1*	Full	**19**	*GNAS*	Full	**34**	*GATA2*	Exon 2
5	*SF3B1*	Full	**20**	*GNB1*	Full	**35**	*KIT*	Exon 8-19, 17
6	*SRSF2*	Full	**21**	*ATM*	Full	**36**	*MPL*	Exon 10
7	*TP53*	Full	**22**	*KRAS*	Full	**37**	*NPM1*	Exon 11
8	*U2AF1*	Full	**23**	*NRAS*	Full	**38**	*PTPN11*	Full
9	*PPM1D*	Full	**24**	*WT1*	Full	**39**	*RUNX1*	Full
10	*CBL*	Full	**25**	*MYD88*	Full	**40**	*SETBP1*	Exon 4-9
11	*IDH1*	Full	**26**	*STAT3*	Full	**41**	*NF1*	Exon 28-38
12	*IDH2*	Full	**27**	*BRCC3*	Full	**42**	*PHF6*	Exon 3-5, 7-9
13	*BCOR*	Full	**28**	*CALR*	Exon 8-9	**43**	*BRAF*	Exon 15
14	*BCORL1*	Full	**29**	*CEBPA*	Full	**44**	*NOTCH1*	Exon 26, 27, 34
15	*EZH2*	Full	**30**	*CSF3R*	Exon 14,17	**45**	*XPO1*	Exon 14

Supplemental Table 2. List of CH mutations detected in the total cohort of 110 patients.

Chr	Pos start	Pos end	ref	var	Gene	Transcript	cdna	aa	ExonicFunc	reads1	reads2	VAF	day
chr2	25234374	25234374	G	A	*DNMT3A*	NM_022552	c.C2644T	p.R882C	nonsynonymous SNV	3228	171	0,0503	0
chr2	25240429	25240429	A	G	*DNMT3A*	NM_022552	c.T2195C	p.F732S	nonsynonymous SNV	2213	157	0,0662	0
chr2	25244267	25244267	G	C	*DNMT3A*	NM_022552	c.C1739G	p.P580R	nonsynonymous SNV	2826	35	0,0122	0
chr2	25241561	25241561	C	T	*DNMT3A*				splicesite	3225	43	0,0132	0
chr2	25234374	25234374	G	A	*DNMT3A*	NM_022552	c.C2644T	p.R882C	nonsynonymous SNV	2010	28	0,0137	0
chr2	25244154	25244154	C	T	*DNMT3A*				splicesite	1132	12	0,0105	0
chr2	25243930	25243930	C	T	*DNMT3A*	NM_022552	c.G1904A	p.R635Q	nonsynonymous SNV	4262	32	0,0075	0
chr2	25246214	25246215	TC	T	*DNMT3A*	NM_022552	c.1374_1375delinsA	p.K459Rfs*192	frameshift substitution	6677	62	0,0092	0
chr2	25239164	25239164	G	A	*DNMT3A*	NM_022552	c.C2374T	p.R792C	nonsynonymous SNV	3490	383	0,0989	0
chr2	25240672	25240672	G	C	*DNMT3A*	NM_022552	c.C2141G	p.S714C	nonsynonymous SNV	6221	33	0,0053	0
chr2	25234380	25234380	T	C	*DNMT3A*	NM_022552	c.A2638G	p.M880V	nonsynonymous SNV	2797	15	0,0053	0
chr2	25240426	25240426	T	C	*DNMT3A*	NM_022552	c.A2198G	p.E733G	nonsynonymous SNV	4795	45	0,0093	0
chr2	25244539	25244539	C	T	*DNMT3A*				splicesite	2758	17	0,0061	0
chr2	25234323	25234323	G	A	*DNMT3A*	NM_022552	c.C2695T	p.R899C	nonsynonymous SNV	2220	22	0,0098	0
chr2	25234374	25234374	G	A	*DNMT3A*	NM_022552	c.C2644T	p.R882C	nonsynonymous SNV	2492	19	0,0076	0
chr2	25247688	25247688	C	T	*DNMT3A*	NM_022552	c.G917A	p.W306X	stopgain	.	.	0,00728	0
chr2	25244315	25244316	TC	T	*DNMT3A*	NM_022552	c.1690_1691delinsA	p.D564Tfs*87	frameshift substitution	.	.	0,0033	0
chr2	25244319	25244319	C	T	*DNMT3A*	NM_022552	c.G1687A	p.V563M	nonsynonymous SNV	.	.	0,00261	0
chr2	25240310	25240310	A	T	*DNMT3A*	NM_022552	c.T2314A	p.F772I	nonsynonymous SNV	.	.	0,00052	0
chr2	25240417	25240417	C	T	*DNMT3A*	NM_022552	c.G2207A	p.R736H	nonsynonymous SNV	4385	627	0,1251	0
chr2	25244214	25244214	G	A	*DNMT3A*	NM_022552	c.C1792T	p.R598X	stopgain	3804	81	0,0208	0
chr2	25240439	25240439	G	C	*DNMT3A*	NM_022552	c.C2185G	p.R729G	nonsynonymous SNV	2853	119	0,04	0
chr2	25241636	25241636	T	TG	*DNMT3A*	NM_022552	c.2008delinsCA	p.I670Hfs*43	frameshift substitution	3806	716	0,1583	0
chr2	25246202	25246202	C	A	*DNMT3A*	NM_022552	c.G1387T	p.E463X	stopgain	3519	73	0,0203	0
chr2	25245317	25245317	C	T	*DNMT3A*	NM_022552	c.G1490A	p.C497Y	nonsynonymous SNV	3806	61	0,0158	0
chr2	25241657	25241658	AG	A	*DNMT3A*	NM_022552	c.1986_1987delinsT	p.S663Rfs*42	frameshift substitution	4361	52	0,0118	0
chr2	25244214	25244214	G	A	*DNMT3A*	NM_022552	c.C1792T	p.R598X	stopgain	3045	32	0,0104	0
chr2	25246159	25246159	C	T	*DNMT3A*				splicesite	2038	249	0,1089	0
chr2	25246667	25246667	A	G	*DNMT3A*	NM_022552	c.T1232C	p.L411P	nonsynonymous SNV	4013	88	0,0215	0
chr2	25234340	25234340	C	G	*DNMT3A*	NM_022552	c.G2678C	p.W893S	nonsynonymous SNV	3377	49	0,0143	0
chr2	25247121	25247122	CA	C	*DNMT3A*	NM_022552	c.1051_1052delinsG	p.C351Afs*56	frameshift substitution	3178	137	0,0413	0
chr2	25244264	25244264	C	G	*DNMT3A*	NM_022552	c.G1742C	p.W581S	nonsynonymous SNV	3972	274	0,0645	0
chr2	25234373	25234373	C	T	*DNMT3A*	NM_022552	c.G2645A	p.R882H	nonsynonymous SNV	2322	28	0,0119	0
chr2	25243933	25243933	A	C	*DNMT3A*	NM_022552	c.T1901G	p.I634S	nonsynonymous SNV	3456	79	0,0223	0
chr2	25247725	25247725	C	A	*DNMT3A*	NM_022552	c.G880T	p.E294X	stopgain	3663	41	0,0111	0

chr2	25240420	25240420	T	C	*DNMT3A*	NM_022552	c.A2204G	p.Y735C	nonsynonymous SNV	2618	89	0,0329	0
chr2	25239199	25239199	A	G	*DNMT3A*	NM_022552	c.T2339C	p.I780T	nonsynonymous SNV	3121	42	0,0133	0
chr2	25246672	25246672	C	T	*DNMT3A*	NM_022552	c.G1227A	p.W409X	stopgain	1700	19	0,0111	0
chr2	25240315	25240315	G	A	*DNMT3A*	NM_022552	c.C2309T	p.S770L	nonsynonymous SNV	1175	24	0,02	0
chr2	25247603	25247604	GC	G	*DNMT3A*	NM_022552	c.1001_1002delinsC	p.G334Afs*11	frameshift substitution	1021	17	0,0164	0
chr2	25240313	25240313	G	A	*DNMT3A*	NM_022552	c.C2311T	p.R771X	stopgain	1019	26	0,0249	0
chr2	25236968	25236968	G	A	*DNMT3A*	NM_022552	c.C2446T	p.Q816X	stopgain	792	31	0,0377	0
chr1	1787387	1787387	C	T	*GNB1*	NM_001282538	c.G667A	p.D223N	nonsynonymous SNV	6655	241	0,0349	0
chrX	130005278	130005278	G	A	*BCORL1*	NM_001184772	c.G47A	p.S16N	nonsynonymous SNV	3607	90	0,0243	0
chr17	60663281	60663281	C	G	*PPM1D*	NM_003620	c.C1547G	p.S516X	stopgain	1761	56	0,0308	0
chr17	60663335	60663340	TTAA(…)	T	*PPM1D*	NM_003620	c.1601_1606delinsT	p.F534Lfs*16	frameshift substitution	1850	36	0,0191	0
chr17	60663359	60663359	A	G	*PPM1D*	NM_003620	c.A1625G	p.N542S	nonsynonymous SNV	1992	42	0,0206	0
chr17	60663388	60663388	C	T	*PPM1D*	NM_003620	c.C1654T	p.R552X	stopgain	2199	24	0,0108	0
chr4	105234499	105234500	AG	A	*TET2*	NM_001127208	c.557_558delinsA	p.S189Vfs*18	frameshift substitution	386	22	0,0539	0
chr17	42322410	42322410	T	C	*STAT3*	NM_001369512	c.A1973G	p.K658R	nonsynonymous SNV	2696	32	0,0117	0
chr17	60663388	60663388	C	T	*PPM1D*	NM_003620	c.C1654T	p.R552X	stopgain	2147	34	0,0156	0
chr7	148811636	148811636	A	T	*EZH2*	NM_001203249	c.T1768A	p.Y590N	nonsynonymous SNV	1351	21	0,0153	0
chr17	60663448	60663448	C	T	*PPM1D*	NM_003620	c.C1714T	p.R572X	stopgain	4398	100	0,0222	0
chr17	60663071	60663071	C	G	*PPM1D*	NM_003620	c.C1337G	p.S446X	stopgain	2136	26	0,012	0
chr20	32435251	32435252	TC	T	*ASXL1*	NM_001363734	c.2356_2357delinsT	p.T787Hfs*19	frameshift substitution	1736	505	0,2252	0
chr4	105236313	105236320	TATT(…)	T	*TET2*	NM_001127208	c.2371_2378delinsT	p.S792Qfs*19	frameshift substitution	1207	440	0,2672	0
chr17	7674221	7674221	G	A	*TP53*	NM_001126115	c.C346T	p.R116W	nonsynonymous SNV	1828	22	0,0119	0
chr17	60663388	60663388	C	T	*PPM1D*	NM_003620	c.C1654T	p.R552X	stopgain	2128	108	0,0483	0
chr9	136496529	136496533	GCTGG	T	*NOTCH1*	NM_017617	c.7206_7210delinsA	p.Q2403Sfs*18	frameshift substitution	2536	1221	0,3212	0
chr11	108315875	108315875	G	A	*ATM*	NM_000051	c.G6059A	p.G2020D	nonsynonymous SNV	1944	37	0,0187	0
chr19	33301825	33301825	G	GGCG(…)	*CEBPA*	NM_001285829	c.233delinsA(…)	p.P77_P78insHP	nonframeshift substit.	1392	57	0,0344	0
chr17	7673803	7673803	G	A	*TP53*	NM_001126115	c.C421T	p.R141C	nonsynonymous SNV	2596	21	0,008	0
chr17	7674894	7674894	G	A	*TP53*	NM_001126115	c.C241T	p.R81X	stopgain	4426	26	0,0058	0
chr17	7674872	7674872	T	C	*TP53*	NM_001126115	c.A263G	p.Y88C	nonsynonymous SNV	4097	28	0,0068	0
chr17	7674262	7674262	T	C	*TP53*	NM_001126115	c.A305G	p.Y102C	nonsynonymous SNV	3202	30	0,0093	0
chr17	7674872	7674872	T	C	*TP53*	NM_001126115	c.A263G	p.Y88C	nonsynonymous SNV	4988	34	0,0068	0
chr17	7675218	7675218	T	C	*TP53*	NM_001126118	c.A277G	p.K93E	nonsynonymous SNV	4300	26	0,006	0
chr11	119278281	119278281	G	A	*CBL*	NM_005188	c.G1211A	p.C404Y	nonsynonymous SNV	2874	29	0,01	0
chr17	60663448	60663448	C	T	*PPM1D*	NM_003620	c.C1714T	p.R572X	stopgain	4541	30	0,0066	0
chr17	60663448	60663448	C	T	*PPM1D*	NM_003620	c.C1714T	p.R572X	stopgain	4372	33	0,0075	0
chr17	60663168	60663168	C	A	*PPM1D*	NM_003620	c.C1434A	p.C478X	stopgain	.	.	0,01358	0
chr20	32434638	32434638	A	AG	*ASXL1*	NM_001363734	c.1743delinsAG	p.G585Wfs*12	frameshift substitution	3525	802	0,1718	0
chr20	32434638	32434638	A	AG	*ASXL1*	NM_001363734	c.1743delinsAG	p.G585Wfs*12	frameshift substitution	2399	152	0,057	0
chr20	32434638	32434638	A	AG	*ASXL1*	NM_001363734	c.1743delinsAG	p.G585Wfs*12	frameshift substitution	1750	636	0,2493	0
chr17	7673704	7673704	G	A	*TP53*	NM_001126115	c.C520T	p.R174X	stopgain	.	.	0,00223	0
chr17	7674872	7674872	T	C	*TP53*	NM_001126115	c.A263G	p.Y88C	nonsynonymous SNV	.	.	0,00192	0
chr21	34859576	34859576	T	C	*RUNX1*	NM_001001890	c.A430G	p.K144E	nonsynonymous SNV	.	.	0,00742	0
chr17	60663015	60663015	G	A	*PPM1D*	NM_003620	c.G1281A	p.W427X	stopgain	1754	39	0,0218	0
chr20	32433453	32433453	A	T	*ASXL1*	NM_001363734	c.A1072T	p.R358X	stopgain	.	.	0,0087	0
chr17	7675095	7675095	C	T	*TP53*	NM_001126115	c.G121A	p.V41M	nonsynonymous SNV	.	.	0,00774	0
chr17	7673776	7673776	G	A	*TP53*	NM_001126115	c.C448T	p.R150W	nonsynonymous SNV	.	.	0,00282	0
chr17	7675075	7675076	AT	A	*TP53*	NM_001126115	c.140_141delinsT	p.H47Lfs*68	frameshift substitution	.	.	0,00031	0
chr17	7676144	7676145	AG	A	*TP53*	NM_001126118	c.107_108delinsT	p.P36Lfs*48	frameshift substitution	.	.	0,00278	0
chr4	105234024	105234025	GA	G	*TET2*	NM_001127208	c.82_83delinsG	p.E28Dfs*21	frameshift substitution	.	.	0,00965	0
chr17	60663201	60663201	T	TTTGA(…)	*PPM1D*	NM_003620	c.1467delinsT(…)	p.T517Ifs*3	frameshift substitution	.	.	0,0094	0
chr17	60663166	60663174	TGCG(…)	T	*PPM1D*	NM_003620	c.1432_1440delinsT	p.A479Pfs*7	frameshift substitution	2305	39	0,0166	0
chr4	105275302	105275302	T	TAGA	*TET2*	NM_001127208	c.4792delinsTAGA	p.Y1598_I2002del	stopgain	.	.	0,00897	0
chr20	32434561	32434561	A	AT	*ASXL1*	NM_001363734	c.1666delinsAT	p.K557*	stopgain	.	.	0,00327	0
chr7	148814109	148814110	GC	G	*EZH2*	NM_001203249	c.1532_1533delinsC	p.C511Sfs*108	frameshift substitution	.	.	0,0097	0
chr20	32434638	32434638	A	AG	*ASXL1*	NM_001363734	c.1743delinsAG	p.G585Wfs*12	frameshift substitution	.	.	0,00815	0
chr11	108331460	108331460	T	A	*ATM*	NM_000051	c.T7532A	p.I2511N	nonsynonymous SNV	.	.	0,00511	0
chr17	60663092	60663092	C	G	*PPM1D*	NM_003620	c.C1358G	p.S453X	stopgain	.	.	0,0056	0
chr20	32434638	32434646	AGGG(…)	A	*ASXL1*	NM_001363734	c.1743_1751delinsA	p.G582Wfs*12	frameshift substitution	.	.	0,00428	0
chr17	42323052	42323052	T	G	*STAT3*	NM_001369512	c.A1840C	p.S614R	nonsynonymous SNV	.	.	0,00391	0
chr17	60663106	60663106	C	T	*PPM1D*	NM_003620	c.C1372T	p.R458X	stopgain	.	.	0,00827	0
chr17	60663262	60663262	C	T	*PPM1D*	NM_003620	c.C1528T	p.Q510X	stopgain	1916	49	0,0249	0
chr17	60663137	60663137	C	G	*PPM1D*	NM_003620	c.C1403G	p.S468X	stopgain	.	.	0,00266	0
chr17	60663262	60663262	C	CA	*PPM1D*	NM_003620	c.1528delinsCA	p.N512Kfs*16	frameshift substitution	.	.	0,00316	0
chr17	60663265	60663265	A	T	*PPM1D*	NM_003620	c.A1531T	p.K511X	stopgain	2047	58	0,0276	0
chr22	28696959	28696959	C	T	*CHEK2*	NM_001349956	c.G836A	p.R279H	nonsynonymous SNV	2050	24	0,0116	0
chr22	28725259	28725259	T	C	*CHEK2*	NM_001349956	c.A428G	p.H143R	nonsynonymous SNV	1685	107	0,0597	0
chr17	60663340	60663341	AG	A	*PPM1D*	NM_003620	c.1606_1607delinsA	p.T537Hfs*2	frameshift substitution	3080	77	0,0244	0
chr22	28734424	28734424	G	A	*CHEK2*	NM_001005735	c.C298T	p.Q100X	stopgain	2732	63	0,0225	0
chr17	7673793	7673793	G	C	*TP53*	NM_001126115	c.C431G	p.A144G	nonsynonymous SNV	5782	94	0,016	0
chr17	7670700	7670700	G	A	*TP53*	NM_001126115	c.C613T	p.R205C	nonsynonymous SNV	4583	166	0,035	0
chr17	60663363	60663364	TG	T	*PPM1D*	NM_003620	c.1629_1630delinsT	p.G544Afs*3	frameshift substitution	4371	88	0,0197	0
chr20	32434599	32434622	TCAC(…)	T	*ASXL1*	NM_001363734	c.1704_1727delinsT	p.E574Rfs*15	frameshift substitution	3358	66	0,0193	0
chr22	28734571	28734571	G	A	*CHEK2*	NM_001005735	c.C151T	p.Q51X	stopgain	5511	96	0,0171	0
chr17	60663182	60663182	C	CT	*PPM1D*	NM_003620	c.1448delinsCT	p.L484Ffs*5	frameshift substitution	4130	199	0,046	0

chr17	60663262	60663262	C	CA	*PPM1D*	NM_003620	c.1528delinsCA	p.N512Kfs*16	frameshift substitution	3949	56	0,0134	0
chr22	28725090	28725090	A	G	*CHEK2*	NM_007194	c.T479C	p.I160T	nonsynonymous SNV	3133	44	0,0138	0
chr17	60656810	60656810	C	CT	*PPM1D*	NM_003620	c.1229delinsCT	p.P411Sfs*23	frameshift substitution	1343	316	0,1909	0
chr4	105243615	105243615	C	T	*TET2*	NM_001127208	c.C3640T	p.R1214W	nonsynonymous SNV	2549	45	0,0173	0
chr4	105243637	105243637	G	T	*TET2*	NM_001127208	c.G3662T	p.C1221F	nonsynonymous SNV	2640	148	0,053	0
chr20	32435592	32435592	G	A	*ASXL1*	NM_001363734	c.G2697A	p.W899X	stopgain	2846	29	0,0101	0
chr11	108330219	108330219	C	A	*ATM*	NM_000051	c.C7313A	p.T2438K	nonsynonymous SNV	2496	56	0,0219	0
chr20	32435034	32435035	AT	A	*ASXL1*	NM_001363734	c.2139_2140delinsA	p.L714*	stopgain	3794	99	0,0254	0
chr20	32435133	32435134	TC	T	*ASXL1*	NM_001363734	c.2238_2239delinsT	p.P747Lfs*10	frameshift substitution	2602	482	0,1562	0
chr20	32435695	32435695	C	CA	*ASXL1*	NM_001363734	c.2800delinsCA	p.H934Qfs*3	frameshift substitution	3666	46	0,0124	0
chr4	105276202	105276202	T	C	*TET2*	NM_001127208	c.T5692C	p.S1898P	nonsynonymous SNV	3454	222	0,0604	0
chr12	25225628	25225628	C	T	*KRAS*	NM_001369786	c.G436A	p.A146T	nonsynonymous SNV	1464	149	0,0924	0
chr17	7674221	7674221	G	A	*TP53*	NM_001126115	c.C346T	p.R116W	nonsynonymous SNV	2942	434	0,1286	0
chr11	108333905	108333905	A	AGAC(…)	*ATM*	NM_000051	c.7947delinsA(…)	p.I2653Tfs*10	frameshift substitution	1769	23	0,0128	0
chr17	60663182	60663184	CTT	C	*PPM1D*	NM_003620	c.1448_1450delinsC	p.L484Kfs*4	frameshift substitution	2398	381	0,1371	0
chr17	60663185	60663185	T	A	*PPM1D*	NM_003620	c.T1451A	p.L484X	stopgain	2386	383	0,1383	0
chr4	105275139	105275140	AC	A	*TET2*	NM_001127208	c.4629_4630delinsA	p.Q1545Sfs*26	frameshift substitution	3205	983	0,2347	0
chr8	116866671	116866671	G	C	*RAD21*	NM_006265	c.C59G	p.A20G	nonsynonymous SNV	3297	54	0,0161	0
chr4	105235662	105235662	C	T	*TET2*	NM_001127208	c.C1720T	p.Q574X	stopgain	2978	33	0,011	0
chr17	7675115	7675115	G	C	*TP53*	NM_001126115	c.C101G	p.S34X	stopgain	7043	303	0,0412	0
chr17	60663014	60663014	G	A	*PPM1D*	NM_003620	c.G1280A	p.W427X	stopgain	1591	36	0,0221	0
chr17	60663340	60663341	AG	A	*PPM1D*	NM_003620	c.1606_1607delinsA	p.T537Hfs*2	frameshift substitution	3318	291	0,0806	0
chr8	116848956	116848956	T	TG	*RAD21*	NM_006265	c.1694delinsCA	p.H565Pfs*9	frameshift substitution	2619	196	0,0697	0
chr4	105237221	105237221	C	CA	*TET2*	NM_001127208	c.3279delinsCA	p.R1095Kfs*9	frameshift substitution	2620	28	0,0106	0
chr2	197402110	197402110	T	C	*SF3B1*	NM_012433	c.A2098G	p.K700E	nonsynonymous SNV	1819	53	0,0283	0
chr17	60663349	60663350	GA	G	*PPM1D*	NM_003620	c.1615_1616delinsG	p.E540Sfs*7	frameshift substitution	2333	43	0,0181	0
chr4	105259626	105259626	T	TG	*TET2*	NM_001127208	c.3811delinsTG	p.C1271Wfs*29	frameshift substitution	1553	52	0,0324	0
chr17	7674180	7674180	C	T	*TP53*				splicesite	2379	53	0,0218	0
chr17	60663388	60663388	C	T	*PPM1D*	NM_003620	c.C1654T	p.R552X	stopgain	4340	78	0,0177	0
chr22	28725043	28725043	C	G	*CHEK2*	NM_007194	c.G526C	p.G176R	nonsynonymous SNV	3197	314	0,0894	0
chr20	32433433	32433433	C	CT	*ASXL1*	NM_001363734	c.1052delinsCT	p.R352Sfs*25	frameshift substitution	3042	267	0,0807	0
chr17	7675109	7675109	T	C	*TP53*	NM_001126115	c.A107G	p.H36R	nonsynonymous SNV	2000	459	0,1867	0
chrX	40062138	40062138	C	T	*BCOR*				splicesite	1557	37	0,0232	0
chr4	105259626	105259626	T	TG	*TET2*	NM_001127208	c.3811delinsTG	p.C1271Wfs*29	frameshift substitution	.	.	0,01921	0
chr7	148828804	148828805	AT	A	*EZH2*	NM_152998	c.443_444delinsT	p.D148Vfs*54	frameshift substitution	.	.	0,01373	0
chr21	34792390	34792390	G	T	*RUNX1*	NM_001001890	c.C1107A	p.F369L	nonsynonymous SNV	.	.	0,01459	0
chr17	7673796	7673796	C	T	*TP53*	NM_001126115	c.G428A	p.C143Y	nonsynonymous SNV	3027	46	0,015	0
chr17	60663148	60663148	G	T	*PPM1D*	NM_003620	c.G1414T	p.E472X	stopgain	3633	54	0,0146	0
chr18	44950097	44950097	G	A	*SETBP1*	NM_015559	c.G757A	p.A253T	nonsynonymous SNV	3799	238	0,059	0
chr17	60663223	60663255	GGCC(…)	G	*PPM1D*	NM_003620	c.1489_1521delinsG	p.G497Dfs*20	frameshift substitution	3530	259	0,0684	0
chr17	60663172	60663172	A	T	*PPM1D*	NM_003620	c.A1438T	p.K480X	stopgain	3015	70	0,0227	0
chr17	60663014	60663014	G	A	*PPM1D*	NM_003620	c.G1280A	p.W427X	stopgain	3247	56	0,017	0
chr17	60663118	60663118	C	T	*PPM1D*	NM_003620	c.C1384T	p.Q462X	stopgain	3901	280	0,067	0
chr17	60663120	60663121	AG	A	*PPM1D*	NM_003620	c.1386_1387delinsA	p.G463Vfs*2	frameshift substitution	4105	52	0,0125	0
chr17	60663148	60663148	G	T	*PPM1D*	NM_003620	c.G1414T	p.E472X	stopgain	3975	55	0,0136	0
chr17	60663166	60663167	TG	T	*PPM1D*	NM_003620	c.1432_1433delinsT	p.C478Sfs*5	frameshift substitution	3885	122	0,0304	0
chr17	60663239	60663239	A	AT	*PPM1D*	NM_003620	c.1505delinsAT	p.S503Ffs*25	frameshift substitution	3784	82	0,0212	0
chr17	60663319	60663320	AC	A	*PPM1D*	NM_003620	c.1585_1586delinsA	p.P530Lfs*9	frameshift substitution	4126	193	0,0447	0
chr22	28725268	28725268	C	G	*CHEK2*	NM_001349956	c.G419C	p.S140T	nonsynonymous SNV	3558	47	0,013	0
chr4	105242834	105242835	GT	G	*TET2*	NM_001127208	c.3501_3502delinsG	p.F1168Lfs*58	frameshift substitution	2212	744	0,2517	0
chr17	60663077	60663077	A	ATT	*PPM1D*	NM_003620	c.1343delinsATT	p.L450Ffs*2	frameshift substitution	3253	60	0,0169	0
chr11	108271395	108271395	T	TG	*ATM*	NM_000051	c.3066delinsTG	p.A1024Sfs*24	frameshift substitution	2373	54	0,0222	0
chr11	108312488	108312488	T	C	*ATM*	NM_000051	c.T5996C	p.I1999T	nonsynonymous SNV	2128	353	0,1423	0
chr17	60663281	60663281	C	A	*PPM1D*	NM_003620	c.C1547A	p.S516X	stopgain	2707	350	0,1145	0
chr20	32434474	32434474	C	T	*ASXL1*	NM_001363734	c.C1579T	p.Q527X	stopgain	2632	319	0,1081	0
chr4	105243621	105243621	C	T	*TET2*	NM_001127208	c.C3646T	p.R1216X	stopgain	3061	35	0,0113	0
chr4	105272680	105272681	AG	A	*TET2*	NM_001127208	c.4299_4300delinsA	p.A1434Lfs*14	frameshift substitution	2073	1549	0,4277	0
chr4	105276080	105276081	CT	C	*TET2*	NM_001127208	c.5570_5571delinsC	p.D1858Tfs*29	frameshift substitution	3016	206	0,0639	0
chr17	42323040	42323040	C	G	*STAT3*	NM_001369512	c.G1852C	p.G618R	nonsynonymous SNV	4859	60	0,0122	0
chr17	60663157	60663157	G	GT	*PPM1D*	NM_003620	c.1423delinsGT	p.E475Vfs*6	frameshift substitution	3249	104	0,0309	0
chr17	60663388	60663388	C	T	*PPM1D*	NM_003620	c.C1654T	p.R552X	stopgain	403	10	0,0242	0
chr17	60663111	60663112	GA	G	*PPM1D*	NM_003620	c.1377_1378delinsG	p.N460Mfs*5	frameshift substitution	1717	57	0,0321	0
chr17	60663171	60663172	TA	T	*PPM1D*	NM_003620	c.1437_1438delinsT	p.A481Pfs*2	frameshift substitution	1619	18	0,011	0
chr17	60663272	60663272	T	TG	*PPM1D*	NM_003620	c.1538delinsTG	p.K514Efs*14	frameshift substitution	911	27	0,0288	0
chr17	60663445	60663445	C	T	*PPM1D*	NM_003620	c.C1711T	p.Q571X	stopgain	3582	89	0,0242	0
chr4	105236965	105236966	AG	A	*TET2*	NM_001127208	c.3023_3024delinsA	p.K1008Nfs*25	frameshift substitution	214	61	0,2218	0
chrX	155116064	155116064	A	T	*BRCC3*	NM_001018055	c.A556T	p.R186X	stopgain	260	24	0,0845	0
chr4	105234763	105234764	TC	T	*TET2*	NM_001127208	c.821_822delinsT	p.N275Ifs*18	frameshift substitution	1366	14	0,0101	0
chr17	60663077	60663078	AT	A	*PPM1D*	NM_003620	c.1343_1344delinsA	p.L450*	stopgain	1900	80	0,0404	0
chr17	42316818	42316818	C	G	*STAT3*	NM_001369512	c.G2228C	p.G743A	nonsynonymous SNV	1398	23	0,0162	0
chr12	112477719	112477719	A	G	*PTPN11*	NM_001330437	c.A922G	p.N308D	nonsynonymous SNV	1076	15	0,0137	0
chr17	60663137	60663137	C	G	*PPM1D*	NM_003620	c.C1403G	p.S468X	stopgain	2030	71	0,0338	0
chr20	32434638	32434646	AGGG(…)	A	*ASXL1*	NM_001363734	c.1743_1751delinsA	p.G582Wfs*12	frameshift substitution	1957	36	0,0178	0
chr2	25241682	25241682	G	GC	*DNMT3A*	NM_022552	c.1962delinsGC	p.I655Hfs*13	frameshift substitution	2857	210	0,0685	30

chr2	25247628	25247628	C	T	*DNMT3A*	NM_022552	c.G977A	p.R326H	nonsynonymous SNV	3192	844	0,2091	30
chr17	60663106	60663106	C	T	*PPM1D*	NM_003620	c.C1372T	p.R458X	stopgain	3166	36	0,0112	30
chr2	25246202	25246202	C	A	*DNMT3A*	NM_022552	c.G1387T	p.E463X	stopgain	2348	81	0,0333	75
chr20	32435592	32435592	G	A	*ASXL1*	NM_001363734	c.G2697A	p.W899X	stopgain	1731	19	0,0109	75
chr4	105276202	105276202	T	C	*TET2*	NM_001127208	c.T5692C	p.S1898P	nonsynonymous SNV	2102	65	0,03	75
chr2	25247688	25247688	C	T	*DNMT3A*	NM_022552	c.G917A	p.W306X	stopgain	3707	38	0,0101	100
chr2	25247725	25247725	C	A	*DNMT3A*	NM_022552	c.G880T	p.E294X	stopgain	2440	82	0,0325	100
chr2	25240426	25240426	T	C	*DNMT3A*	NM_022552	c.A2198G	p.E733G	nonsynonymous SNV	2039	6	0,00293	100
chr2	25234373	25234373	C	T	*DNMT3A*	NM_022552	c.G2645A	p.R882H	nonsynonymous SNV	2786	18	0,0064	100
chr2	25243933	25243933	A	C	*DNMT3A*	NM_022552	c.T1901G	p.I634S	nonsynonymous SNV	3094	85	0,0267	100
chr2	25240672	25240672	G	C	*DNMT3A*	NM_022552	c.C2141G	p.S714C	nonsynonymous SNV	3268	30	0,0091	100
chr2	25239164	25239164	G	A	*DNMT3A*	NM_022552	c.C2374T	p.R792C	nonsynonymous SNV	1669	199	0,1065	100
chr2	25244315	25244316	TC	T	*DNMT3A*	NM_022552	c.1690_1691delinsA	p.D564Tfs*87	frameshift substitution	1312	19	0,0143	100
chr2	25244319	25244319	C	T	*DNMT3A*	NM_022552	c.G1687A	p.V563M	nonsynonymous SNV	2349	26	0,0109	100
chr2	25240420	25240420	T	C	*DNMT3A*	NM_022552	c.A2204G	p.Y735C	nonsynonymous SNV	1929	66	0,0331	100
chr2	25236968	25236968	G	A	*DNMT3A*	NM_022552	c.C2446T	p.Q816X	stopgain	1597	69	0,0414	100
chr17	7670700	7670700	G	A	*TP53*	NM_001126115	c.C613T	p.R205C	nonsynonymous SNV	1924	494	0,2043	100
chr17	7673704	7673704	G	A	*TP53*	NM_001126115	c.C520T	p.R174X	stopgain	2080	36	0,017	100
chr17	7674872	7674872	T	C	*TP53*	NM_001126115	c.A263G	p.Y88C	nonsynonymous SNV	2526	45	0,0175	100
chr17	7675115	7675115	G	C	*TP53*	NM_001126115	c.C101G	p.S34X	stopgain	2663	802	0,2313	100
chr21	34859576	34859576	T	C	*RUNX1*	NM_001001890	c.A430G	p.K144E	nonsynonymous SNV	1982	59	0,0289	100
chrX	40062138	40062138	C	T	*BCOR*				splicesite	696	31	0,0426	100
chr17	60663171	60663172	TA	T	*PPM1D*	NM_003620	c.1437_1438delinsT	p.A481Pfs*2	frameshift substitution	1331	31	0,0228	100
chr17	60663272	60663272	T	TG	*PPM1D*	NM_003620	c.1538delinsTG	p.K514Efs*14	frameshift substitution	794	36	0,0434	100
chr4	105236965	105236966	AG	A	*TET2*	NM_001127208	c.3023_3024delinsA	p.K1008Nfs*25	frameshift substitution	846	476	0,49635	100
chrX	155116064	155116064	A	T	*BRCC3*	NM_001018055	c.A556T	p.R186X	stopgain	984	289	0,2249	100
chr20	32433453	32433453	A	T	*ASXL1*	NM_001363734	c.A1072T	p.R358X	stopgain	2510	55	0,0214	100
chr4	105234763	105234764	TC	T	*TET2*	NM_001127208	c.821_822delinsT	p.N275Ifs*18	frameshift substitution	2249	23	0,0101	100
chr17	7675095	7675095	C	T	*TP53*	NM_001126115	c.G121A	p.V41M	nonsynonymous SNV	1904	21	0,0109	100
chr17	60663077	60663078	AT	A	*PPM1D*	NM_003620	c.1343_1344delinsA	p.L450*	stopgain	1865	78	0,0401	100
chr17	7675075	7675076	AT	A	*TP53*	NM_001126115	c.140_141delinsT	p.H47Lfs*68	frameshift substitution	2925	1	0,00032	100
chr17	7675178	7675178	A	T	*TP53*	NM_001126115	c.T38A	p.L13Q	nonsynonymous SNV	2807	1	0,00035	100
chr17	7673776	7673776	G	A	*TP53*	NM_001126115	c.C448T	p.R150W	nonsynonymous SNV	2088	13	0,0061	100
chr17	60663014	60663014	G	A	*PPM1D*	NM_003620	c.G1280A	p.W427X	stopgain	1125	11	0,00951	100
chr17	60663118	60663118	C	T	*PPM1D*	NM_003620	c.C1384T	p.Q462X	stopgain	1490	18	0,0117	100
chr17	60663120	60663121	AG	A	*PPM1D*	NM_003620	c.1386_1387delinsA	p.G463Vfs*2	frameshift substitution	1511	1	0,00065	100
chr17	60663148	60663148	G	T	*PPM1D*	NM_003620	c.G1414T	p.E472X	stopgain	1535	14	0,00885	100
chr17	60663166	60663167	TG	T	*PPM1D*	NM_003620	c.1432_1433delinsT	p.C478Sfs*5	frameshift substitution	1530	9	0,00569	100
chr17	60663239	60663239	A	AT	*PPM1D*	NM_003620	c.1505delinsAT	p.S503Ffs*25	frameshift substitution	1218	13	0,0106	100
chr17	60663319	60663320	AC	A	*PPM1D*	NM_003620	c.1585_1586delinsA	p.P530Lfs*9	frameshift substitution	1247	15	0,0119	100
chr17	60663448	60663448	C	T	*PPM1D*	NM_003620	c.C1714T	p.R572X	stopgain	1393	21	0,0149	100
chr17	7676144	7676145	AG	A	*TP53*	NM_001126118	c.107_108delinsT	p.P36Lfs*48	frameshift substitution	2215	11	0,00487	100
chr20	32434638	32434638	A	AG	*ASXL1*	NM_001363734	c.1743delinsAG	p.G585Wfs*12	frameshift substitution	1175	171	0,1171	100
chr4	105242834	105242835	GT	G	*TET2*	NM_001127208	c.3501_3502delinsG	p.F1168Lfs*58	frameshift substitution	935	183	0,19063	100
chr11	108271395	108271395	T	TG	*ATM*	NM_000051	c.3066delinsTG	p.A1024Sfs*24	frameshift substitution	675	71	0,0952	100
chr11	108312488	108312488	T	C	*ATM*	NM_000051	c.T5996C	p.I1999T	nonsynonymous SNV	532	142	0,2107	100
chr17	60663281	60663281	C	A	*PPM1D*	NM_003620	c.C1547A	p.S516X	stopgain	1066	147	0,1212	100
chr20	32434474	32434474	C	T	*ASXL1*	NM_001363734	c.C1579T	p.Q527X	stopgain	866	246	0,221	100
chr4	105243621	105243621	C	T	*TET2*	NM_001127208	c.C3646T	p.R1216X	stopgain	1467	5	0,00338	100
chr4	105272680	105272681	AG	A	*TET2*	NM_001127208	c.4299_4300delinsA	p.A1434Lfs*14	frameshift substitution	794	761	0,48043	100
chr4	105276080	105276081	CT	C	*TET2*	NM_001127208	c.5570_5571delinsC	p.D1858Tfs*29	frameshift substitution	1735	45	0,02468	100
chr17	7675109	7675109	T	C	*TP53*	NM_001126115	c.A107G	p.H36R	nonsynonymous SNV	2134	663	0,2367	100
chr4	105234024	105234025	GA	G	*TET2*	NM_001127208	c.82_83delinsG	p.E28Dfs*21	frameshift substitution	2283	16	0,0069	100
chr3	128486323	128486323	C	T	*GATA2*	NM_001145662	c.G275A	p.S92N	nonsynonymous SNV	2087	45	0,0211	100
chr17	7673796	7673796	C	T	*TP53*	NM_001126115	c.G428A	p.C143Y	nonsynonymous SNV	3012	36	0,0118	100
chr17	60663148	60663148	G	T	*PPM1D*	NM_003620	c.G1414T	p.E472X	stopgain	2677	36	0,0133	100
chr17	60663201	60663201	T	TTTG(…)	*PPM1D*	NM_003620	c.1467delinsT(…)	p.T517Ifs*3	frameshift substitution	1099	68	0,0275	100
chr4	105259626	105259626	T	TG	*TET2*	NM_001127208	c.3811delinsTG	p.C1271Wfs*29	frameshift substitution	1942	38	0,0192	100
chr7	148828804	148828805	AT	A	*EZH2*	NM_152998	c.443_444delinsT	p.D148Vfs*54	frameshift substitution	2259	45	0,0195	100
chr17	42322402	42322402	C	A	*STAT3*	NM_001369512	c.G1981T	p.D661Y	nonsynonymous SNV	3319	29	0,0087	100
chr21	34792390	34792390	G	T	*RUNX1*	NM_001001890	c.C1107A	p.F369L	nonsynonymous SNV	2096	18	0,0084	100
chr4	105275302	105275302	T	TAGA	*TET2*	NM_001127208	c.4792delinsTAGA	p.Y1598_I2002del	stopgain	3431	15	0,0043	100
chr17	60663223	60663255	GGCC(…)	G	*PPM1D*	NM_003620	c.1489_1521delinsG	p.G497Dfs*20	frameshift substitution	1949	198	0,0922	100
chr7	148814109	148814110	GC	G	*EZH2*	NM_001203249	c.1532_1533delinsC	p.C511Sfs*108	frameshift substitution	2321	25	0,0107	100
chr20	32434561	32434561	A	AT	*ASXL1*	NM_001363734	c.1666delinsAT	p.K557*	stopgain	2460	21	0,00809	100
chr20	32434638	32434638	A	AG	*ASXL1*	NM_001363734	c.1743delinsAG	p.G585Wfs*12	frameshift substitution	2637	36	0,01338	100
chr11	108331460	108331460	T	A	*ATM*	NM_000051	c.T7532A	p.I2511N	nonsynonymous SNV	756	14	0,0182	100
chr17	60663015	60663015	G	A	*PPM1D*	NM_003620	c.G1281A	p.W427X	stopgain	1175	45	0,0368	100
chr17	60663166	60663174	TGCG(…)	T	*PPM1D*	NM_003620	c.1432_1440delinsT	p.A479Pfs*7	frameshift substitution	1425	32	0,022	100
chr17	60663168	60663168	C	A	*PPM1D*	NM_003620	c.C1434A	p.C478X	stopgain	1403	21	0,0145	100
chr17	60663262	60663262	C	T	*PPM1D*	NM_003620	c.C1528T	p.Q510X	stopgain	1151	43	0,036	100
chr17	60663265	60663265	A	T	*PPM1D*	NM_003620	c.A1531T	p.K511X	stopgain	1166	60	0,0489	100
chr22	28725259	28725259	T	C	*CHEK2*	NM_001349956	c.A428G	p.H143R	nonsynonymous SNV	1018	64	0,0591	100
chr22	28696959	28696959	C	T	*CHEK2*	NM_001349956	c.G836A	p.R279H	nonsynonymous SNV	1280	6	0,00462	100

chr17	7673803	7673803	G	A	*TP53*	NM_001126115	c.C421T	p.R141C	nonsynonymous SNV	2080	15	0,0072	100
chr22	28734571	28734571	G	A	*CHEK2*	NM_001005735	c.C151T	p.Q51X	stopgain	2979	107	0,0347	100
chr17	7674262	7674262	T	C	*TP53*	NM_001126115	c.A305G	p.Y102C	nonsynonymous SNV	1848	15	0,0081	100
chr17	60663092	60663092	C	G	*PPM1D*	NM_003620	c.C1358G	p.S453X	stopgain	1700	87	0,0487	100
chr20	32434638	32434646	AGGG(…)	A	*ASXL1*	NM_001363734	c.1743_1751delinsA	p.G582Wfs*12	frameshift substitution	1579	52	0,0313	100
chr17	42323052	42323052	T	G	*STAT3*	NM_001369512	c.A1840C	p.S614R	nonsynonymous SNV	2506	38	0,0149	100
chr17	60663106	60663106	C	T	*PPM1D*	NM_003620	c.C1372T	p.R458X	stopgain	1095	36	0,0318	100
chr17	60663137	60663137	C	G	*PPM1D*	NM_003620	c.C1403G	p.S468X	stopgain	1965	31	0,0152	100
chr17	60663172	60663172	A	T	*PPM1D*	NM_003620	c.A1438T	p.K480X	stopgain	1752	193	0,0992	100
chr17	60663262	60663262	C	CA	*PPM1D*	NM_003620	c.1528delinsCA	p.N512Kfs*16	frameshift substitution	1497	10	0,0064	100
chr17	60663349	60663350	GA	G	*PPM1D*	NM_003620	c.1615_1616delinsG	p.E540Sfs*7	frameshift substitution	4040	39	0,00958	100
chr4	105259626	105259626	T	TG	*TET2*	NM_001127208	c.3811delinsTG	p.C1271Wfs*29	frameshift substitution	2903	112	0,03816	100
chr4	105234499	105234500	AG	A	*TET2*	NM_001127208	c.557_558delinsA	p.S189Vfs*18	frameshift substitution	2842	108	0,0366	100
chr8	116866671	116866671	G	C	*RAD21*	NM_006265	c.C59G	p.A20G	nonsynonymous SNV	3434	77	0,0219	100
chr11	119278281	119278281	G	A	*CBL*	NM_005188	c.G1211A	p.C404Y	nonsynonymous SNV	2952	14	0,00469	100
chr17	60663077	60663077	A	ATT	*PPM1D*	NM_003620	c.1343delinsATT	p.L450Ffs*2	frameshift substitution	2077	9	0,00422	100
chr17	60663157	60663157	G	GT	*PPM1D*	NM_003620	c.1423delinsGT	p.E475Vfs*6	frameshift substitution	2123	20	0,0092	100
chr17	60663182	60663184	CTT	C	*PPM1D*	NM_003620	c.1448_1450delinsC	p.L484Kfs*4	frameshift substitution	2334	927	0,2836	100
chr17	60663185	60663185	T	A	*PPM1D*	NM_003620	c.T1451A	p.L484X	stopgain	2329	930	0,2853	100
chr17	60663262	60663262	C	CA	*PPM1D*	NM_003620	c.1528delinsCA	p.N512Kfs*16	frameshift substitution	3561	49	0,0136	100
chr4	105275139	105275140	AC	A	*TET2*	NM_001127208	c.4629_4630delinsA	p.Q1545Sfs*26	frameshift substitution	3435	1825	0,347	100
chr2	25240426	25240426	T	C	*DNMT3A*	NM_022552	c.A2198G	p.E733G	nonsynonymous SNV	960	8	0,0083	200
chr2	25234373	25234373	C	T	*DNMT3A*	NM_022552	c.G2645A	p.R882H	nonsynonymous SNV	1343	33	0,024	200
chr2	25243933	25243933	A	C	*DNMT3A*	NM_022552	c.T1901G	p.I634S	nonsynonymous SNV	2371	28	0,01155	200
chr2	25247725	25247725	C	A	*DNMT3A*	NM_022552	c.G880T	p.E294X	stopgain	1884	51	0,02621	200
chr2	25240420	25240420	T	C	*DNMT3A*	NM_022552	c.A2204G	p.Y735C	nonsynonymous SNV	1420	65	0,0438	200
chr17	60663171	60663172	TA	T	*PPM1D*	NM_003620	c.1437_1438delinsT	p.A481Pfs*2	frameshift substitution	1359	16	0,0116	200
chr17	60663272	60663272	T	TG	*PPM1D*	NM_003620	c.1538delinsTG	p.K514Efs*14	frameshift substitution	786	19	0,0236	200
chr17	60663014	60663014	G	A	*PPM1D*	NM_003620	c.G1280A	p.W427X	stopgain	1739	16	0,00904	200
chr17	60663118	60663118	C	T	*PPM1D*	NM_003620	c.C1384T	p.Q462X	stopgain	1993	21	0,01038	200
chr17	60663148	60663148	G	T	*PPM1D*	NM_003620	c.G1414T	p.E472X	stopgain	2062	28	0,01328	200
chr17	60663166	60663167	TG	T	*PPM1D*	NM_003620	c.1432_1433delinsT	p.C478Sfs*5	frameshift substitution	2071	3	0,00143	200
chr17	60663239	60663239	A	AT	*PPM1D*	NM_003620	c.1505delinsAT	p.S503Ffs*25	frameshift substitution	1999	11	0,00545	200
chr17	60663319	60663320	AC	A	*PPM1D*	NM_003620	c.1585_1586delinsA	p.P530Lfs*9	frameshift substitution	2132	34	0,01579	200
chr17	60663448	60663448	C	T	*PPM1D*	NM_003620	c.C1714T	p.R572X	stopgain	2242	29	0,01266	200
chr17	7676144	7676145	AG	A	*TP53*	NM_001126118	c.107_108delinsT	p.P36Lfs*48	frameshift substitution	3072	10	0,00323	200
chr20	32434638	32434638	A	AG	*ASXL1*	NM_001363734	c.1743delinsAG	p.G585Wfs*12	frameshift substitution	2632	459	0,17308	200
chr4	105242834	105242835	GT	G	*TET2*	NM_001127208	c.3501_3502delinsG	p.F1168Lfs*58	frameshift substitution	1187	308	0,20699	200
chr4	105234024	105234025	GA	G	*TET2*	NM_001127208	c.82_83delinsG	p.E28Dfs*21	frameshift substitution	1652	19	0,0114	200
chr17	7673796	7673796	C	T	*TP53*	NM_001126115	c.G428A	p.C143Y	nonsynonymous SNV	1430	20	0,0138	200
chr17	42322402	42322402	C	A	*STAT3*	NM_001369512	c.G1981T	p.D661Y	nonsynonymous SNV	1556	36	0,0226	200
chr17	60663148	60663148	G	T	*PPM1D*	NM_003620	c.G1414T	p.E472X	stopgain	1189	27	0,0222	200
chr17	60663201	60663201	T	TTTG(…)	*PPM1D*	NM_003620	c.1467delinsT(…)	p.T517Ifs*3	frameshift substitution	481	116	0,1022	200
chr21	34792390	34792390	G	T	*RUNX1*	NM_001001890	c.C1107A	p.F369L	nonsynonymous SNV	1416	43	0,0295	200
chr4	105259626	105259626	T	TG	*TET2*	NM_001127208	c.3811delinsTG	p.C1271Wfs*29	frameshift substitution	880	29	0,0319	200
chr4	105275302	105275302	T	TAGA	*TET2*	NM_001127208	c.4792delinsTAGA	p.Y1598_I2002del	stopgain	1319	15	0,0112	200
chr7	148828804	148828805	AT	A	*EZH2*	NM_152998	c.443_444delinsT	p.D148Vfs*54	frameshift substitution	825	47	0,0539	200
chr20	32434561	32434561	A	AT	*ASXL1*	NM_001363734	c.1666delinsAT	p.K557*	stopgain	1597	27	0,0166	200
chr17	60663223	60663255	GGCC(…)	G	*PPM1D*	NM_003620	c.1489_1521delinsG	p.G497Dfs*20	frameshift substitution	1203	82	0,0638	200
chr20	32434638	32434638	A	AG	*ASXL1*	NM_001363734	c.1743delinsAG	p.G585Wfs*12	frameshift substitution	1361	71	0,0454	200
chr7	148814109	148814110	GC	G	*EZH2*	NM_001203249	c.1532_1533delinsC	p.C511Sfs*108	frameshift substitution	1524	12	0,00768	200
chr22	28734571	28734571	G	A	*CHEK2*	NM_001005735	c.C151T	p.Q51X	stopgain	2090	44	0,0206	200
chr17	7674262	7674262	T	C	*TP53*	NM_001126115	c.A305G	p.Y102C	nonsynonymous SNV	1500	5	0,00322	200
chr17	7673776	7673776	G	A	*TP53*	NM_001126115	c.C448T	p.R150W	nonsynonymous SNV	1632	9	0,00544	200
chr17	7675075	7675076	AT	A	*TP53*	NM_001126115	c.140_141delinsT	p.H47Lfs*68	frameshift substitution	1711	2	0,00114	200
chr17	7675178	7675178	A	T	*TP53*	NM_001126115	c.T38A	p.L13Q	nonsynonymous SNV	1665	2	0,00119	200
chr2	25247725	25247725	C	A	*DNMT3A*	NM_022552	c.G880T	p.E294X	stopgain	1436	21	0,0144	365
chr2	25243933	25243933	A	C	*DNMT3A*	NM_022552	c.T1901G	p.I634S	nonsynonymous SNV	1217	21	0,017	365
chr2	25240310	25240310	A	T	*DNMT3A*	NM_022552	c.T2314A	p.F772I	nonsynonymous SNV	2294	246	0,0968	365
chr2	25240420	25240420	T	C	*DNMT3A*	NM_022552	c.A2204G	p.Y735C	nonsynonymous SNV	1464	17	0,01086	365
chr17	7675075	7675076	AT	A	*TP53*	NM_001126115	c.140_141delinsT	p.H47Lfs*68	frameshift substitution	1661	47	0,0275	365
chr17	7675178	7675178	A	T	*TP53*	NM_001126115	c.T38A	p.L13Q	nonsynonymous SNV	1616	21	0,0128	365
chr17	7673776	7673776	G	A	*TP53*	NM_001126115	c.C448T	p.R150W	nonsynonymous SNV	1447	9	0,0062	365
chr17	60663014	60663014	G	A	*PPM1D*	NM_003620	c.G1280A	p.W427X	stopgain	2518	12	0,00472	365
chr17	60663118	60663118	C	T	*PPM1D*	NM_003620	c.C1384T	p.Q462X	stopgain	3045	28	0,00904	365
chr17	60663120	60663121	AG	A	*PPM1D*	NM_003620	c.1386_1387delinsA	p.G463Vfs*2	frameshift substitution	3037	2	0,00065	365
chr17	60663239	60663239	A	AT	*PPM1D*	NM_003620	c.1505delinsAT	p.S503Ffs*25	frameshift substitution	2528	19	0,00743	365
chr17	60663319	60663320	AC	A	*PPM1D*	NM_003620	c.1585_1586delinsA	p.P530Lfs*9	frameshift substitution	2936	66	0,02231	365
chr17	60663148	60663148	G	T	*PPM1D*	NM_003620	c.G1414T	p.E472X	stopgain	2861	73	0,0127	365
chr17	60663166	60663167	TG	T	*PPM1D*	NM_003620	c.1432_1433delinsT	p.C478Sfs*5	frameshift substitution	2867	27	0,00933	365
chr17	7676144	7676145	AG	A	*TP53*	NM_001126118	c.107_108delinsT	p.P36Lfs*48	frameshift substitution	3964	11	0,00276	365
chr4	105242834	105242835	GT	G	*TET2*	NM_001127208	c.3501_3502delinsG	p.F1168Lfs*58	frameshift substitution	1858	442	0,23586	365
chr17	60663448	60663448	C	T	*PPM1D*	NM_003620	c.C1714T	p.R572X	stopgain	3335	31	0,00913	365
chr20	32434638	32434638	A	AG	*ASXL1*	NM_001363734	c.1743delinsAG	p.G585Wfs*12	frameshift substitution	3278	531	0,16057	365

chr17	7673796	7673796	C	T	*TP53*	NM_001126115	c.G428A	p.C143Y	nonsynonymous SNV	1458	25	0,0169	365
chr17	42322402	42322402	C	A	*STAT3*	NM_001369512	c.G1981T	p.D661Y	nonsynonymous SNV	1473	138	0,0856	365
chr17	60663148	60663148	G	T	*PPM1D*	NM_003620	c.G1414T	p.E472X	stopgain	1026	15	0,0144	365
chr17	60663201	60663201	T	TTTG(…)	*PPM1D*	NM_003620	c.1467delinsT(…)	p.T517Ifs*3	frameshift substitution	369	12	0,0147	365
chr4	105259626	105259626	T	TG	*TET2*	NM_001127208	c.3811delinsTG	p.C1271Wfs*29	frameshift substitution	793	81	0,0928	365
chr7	148828804	148828805	AT	A	*EZH2*	NM_152998	c.443_444delinsT	p.D148Vfs*54	frameshift substitution	686	16	0,0228	365
chr21	34792390	34792390	G	T	*RUNX1*	NM_001001890	c.C1107A	p.F369L	nonsynonymous SNV	828	8	0,00945	365
chr4	105275302	105275302	T	TAGA	*TET2*	NM_001127208	c.4792delinsTAGA	p.Y1598_I2002del	stopgain	1335	7	0,00502	365
chr17	60663223	60663255	GGCC(…)	G	*PPM1D*	NM_003620	c.1489_1521delinsG	p.G497Dfs*20	frameshift substitution	495	91	0,1553	365
chr20	32434561	32434561	A	AT	*ASXL1*	NM_001363734	c.1666delinsAT	p.K557*	stopgain	469	10	0,0209	365
chr7	148814109	148814110	GC	G	*EZH2*	NM_001203249	c.1532_1533delinsC	p.C511Sfs*108	frameshift substitution	896	10	0,011	365
chr20	32434638	32434638	A	AG	*ASXL1*	NM_001363734	c.1743delinsAG	p.G585Wfs*12	frameshift substitution	269	25	0,0812	365
chr17	60663014	60663014	G	A	*PPM1D*	NM_003620	c.G1280A	p.W427X	stopgain	2548	12	0,00465	365
chr2	197402110	197402110	T	C	*SF3B1*	NM_012433	c.A2098G	p.K700E	nonsynonymous SNV	2391	81	0,0328	365
chr2	25240310	25240310	A	T	*DNMT3A*	NM_022552	c.T2314A	p.F772I	nonsynonymous SNV	2589	10	0,00379	700
chr17	60663014	60663014	G	A	*PPM1D*	NM_003620	c.G1280A	p.W427X	stopgain	2425	12	0,0049	700
chr2	197402110	197402110	T	C	*SF3B1*	NM_012433	c.A2098G	p.K700E	nonsynonymous SNV	1706	777	0,3129	700
chr17	60663239	60663239	A	AT	*PPM1D*	NM_003620	c.1505delinsAT	p.S503Ffs*25	frameshift substitution	1038	5	0,00451	730
chr17	60663118	60663118	C	T	*PPM1D*	NM_003620	c.C1384T	p.Q462X	stopgain	1553	4	0,00244	730
chr17	60663120	60663121	AG	A	*PPM1D*	NM_003620	c.1386_1387delinsA	p.G463Vfs*2	frameshift substitution	1544	2	0,00123	730
chr17	60663319	60663320	AC	A	*PPM1D*	NM_003620	c.1585_1586delinsA	p.P530Lfs*9	frameshift substitution	607	14	0,02184	730
chr17	7676144	7676145	AG	A	*TP53*	NM_001126118	c.107_108delinsT	p.P36Lfs*48	frameshift substitution	1157	12	0,0103	730
chr17	60663148	60663148	G	T	*PPM1D*	NM_003620	c.G1414T	p.E472X	stopgain	1157	25	0,0212	730
chr17	60663448	60663448	C	T	*PPM1D*	NM_003620	c.C1714T	p.R572X	stopgain	784	11	0,0138	730
chr4	105242834	105242835	GT	G	*TET2*	NM_001127208	c.3501_3502delinsG	p.F1168Lfs*58	frameshift substitution	882	219	0,24524	730
chr20	32434638	32434638	A	AG	*ASXL1*	NM_001363734	c.1743delinsAG	p.G585Wfs*12	frameshift substitution	273	55	0,1608	730

Abbreviations: *aa*= amino acid; *Pos*=position *VAF*= variant allele frequency*; ref*: reference *var*: variation

Supplemental Table 3. Patient characteristics according to CH with low and high VAF.

Characteristic n=62	A: CH positive VAF 1-5% n=35	B: CH positive VAF >5% n=27	P-value* A vs B
Age at diagnosis, years			0.59**
Median (range)	61 (37-75)	63 (17-76)	
Age at CAR T- treatment, years			0.91**
Median (range)	64 (40-79)	66 (21-77)	
Sex			1.0
Male - no. (%)	26 (74)	20 (74)	
Female - no. (%)	9 (26)	7 (26)	
Diagnosis			
LBCL- no. (%)	30 (86)	17 (67)	
TFL - no. (%)	2 (6)	3 (11)	
MCL- no. (%)	3 (7)	4 (15)	
ALL - no. (%)	0	2 (7)	
Ann- Arbor Stage			0.77
I-II- no. (%)	8 (23)	7 (26)	
III-IV- no. (%)	26 (74)	18 (67)	
Missing data- no. (%)	1 (3)	2 (7)	
Prior lines of therapy			0.96
Median (range)	4 (2-8)	4 (2-9)	
Autologous HSCT prior CAR T- cell treatment			0.43
yes- no. (%)	11 (31)	12 (44)	
no- no. (%)	24 (69)	15 (56)	
CNS involvement prior CAR T- cell treatment			1.0
yes- no. (%)	7 (20)	5 (19)	
no- no. (%)	28 (80)	22 (82)	
Remission prior CAR T- cell treatment (CR/PR vs. SD/PD)			0.2

CR- no. (%)	1 (3)	5 (19)	
PR- no. (%)	10 (29)	8 (30)	
SD- no. (%)	4 (11)	6 (22)	
PD - no. (%)	20 (57)	8 (30)	
CAR T- cell product			
Axicabtagene ciloleucel - no. (%)	17 (49)	7 (26)	
Tisagenlecleucel- no. (%)	15 (43)	16 (69)	
Brexucabtagene autoleucel - no. (%)	3 (9)	4 (15)	

Abbreviations: *CH*= clonal hematopoiesis; *LBCL*= large B-cell lymphomas; *TFL*= transformed follicular lymphoma; *MCL*= mantle cell lymphoma; *ALL*= acute lymphoblastic leukaemia; *CR*= complete remission; *PR*= partial remission; *SD*= stable disease; *PD*= progressive disease; *HSCT*= hematopoietic stem cell transplantation; *CNS*= central nervous system *no*.=number *VAF*= variant allele frequency **Statistics: *)** calculated with Fisher's exact test, missing data were excluded ****)** calculated with Mann Whitney U test

Supplemental Table 4. Prevalence of the most frequent CH mutations depending on prior high-dose chemotherapy with autologous or allogeneic HCT (n=109 patients with available information).

Prevalence of mutations VAF cutoff 1%	**High-dose chemotherapy prior CAR T-cell therapy Yes (n=45)**	**High-dose chemotherapy prior CAR T-cell therapy No (n=64)**	**P**
***DNMT3A*, n=26**	13 (29%)	13 (20%)	0.36
***TET2*, n=13**	8 (18%)	5 (8%)	0.14
***ASXL1*, n=9**	6 (13%)	3 (5%)	0.16
***PPM1D*, n=28**	10 (22%)	18 (28%)	0.51
***TP53*, n=7**	3 (7%)	4 (6%)	1.0

Supplemental Table 5. Prevalence of the most frequent CH mutations depending on prior platinum-based chemotherapy (oxaliplatin, cisplatin; n=107 patients with available information).

Prevalence of mutations VAF cutoff 1%	**Platinum derivatives prior CAR T-cell therapy Yes (n=92)**	**Platinum derivatives prior CAR T-cell therapy No (n=15)**	**P**
***DNMT3A*, n=26**	21 (23%)	5 (33%)	0.52
***TET2*, n=13**	10 (11%)	3 (20%)	0.39
***ASXL1*, n=9**	9 (10%)	0 (0%)	0.35
***PPM1D*, n=27**	27 (29%)	0 (0%)	0.01
***TP53*, n=7**	6 (7%)	1 (7%)	1.0

Supplemental Table 6. Prevalence of the most frequent CH mutations depending on prior therapy with topoisomerase II inhibitors (etoposide; n=107 patients with available information).

Prevalence of mutations VAF cutoff 1%	**Top II inhibitors prior CAR T-cell therapy Yes (n=55)**	**Top II inhibitors prior CAR T-cell therapy No (n=52)**	**P**
***DNMT3A*, n=26**	9 (16%)	17 (33%)	0.07
***TET2*, n=13**	6 (11%)	7 (14%)	0.77
***ASXL1*, n=9**	7 (13%)	2 (4%)	0.16
***PPM1D*, n=27**	15 (27%)	12 (23%)	0.66
***TP53*, n=7**	6 (11%)	1 (2%)	0.11

Supplemental Table 7. Prevalence of the most frequent CH mutations depending on prior therapy with antimetabolites (cytarabine, gemcitabine, mercaptopurine; n=107 patients with available information).

Prevalence of mutations **VAF cutoff 1%**	**Antimetabolites** **prior CAR T-cell therapy** **Yes (n=99)**	**Antimetabolites** **prior CAR T-cell therapy** **No (n=8)**	**P**
***DNMT3A*, n=26**	25 (25%)	1 (13%)	0.68
***TET2*, n=13**	12 (12%)	1 (13%)	1.0
***ASXL1*, n=9**	9 (9%)	0 (0%)	1.0
***PPM1D*, n=27**	25 (25%)	2 (25%)	1.0
***TP53*, n=7**	6 (6%)	1 (13%)	0.43

Supplemental Table 8. Prevalence of the most frequent CH mutations depending on prior autoHCT treatment (n=110 patients).

Prevalence of mutations **VAF cutoff 1%**	**auto SCT** **prior CAR T-cell therapy** **Yes (n=37)**	**auto SCT** **prior CAR T-cell therapy** **No (n=73)**	**P**
CH in any gene, n=62	23 (62%)	39 (53%)	
***DNMT3A*, n=26**	10 (27%)	16 (22%)	0.64
***TET2*, n=13**	8 (22%)	5 (7%)	0.03
***ASXL1*, n=9**	6 (16%)	3 (4%)	0.05
***PPM1D*, n=28**	9 (24%)	19 (26%)	1.0
***TP53*, n=7**	2 (5%)	5 (7%)	1.0

Supplemental Table 9. CRS and ICANS frequency according to presence or absence of CH.

Toxicity	A: Total Cohort n=110	B: CH negative n=48	C: CH positive n=62	P-value* B vs C
CRS no. (%)				0.68
no onset	**33 (30.0)**	**13 (27.1)**	**20 (32.3)**	
onset	**77 (70.0)**	**35 (72.9)**	**42 (67.7)**	
CRS Grading no. (% of onset)				
Grade I	24 (31.2)	12 (34.3)	12 (28.6)	
Grade II	45 (58.4)	18 (51.4)	27 (64.3)	
Grade III	7 (9.0)	4 (11.4)	3 (7.1)	
Grade IV	1 (1.3)	1 (2.9)	0 (0)	
Grade ≥II	53 (68.8)	23 (65.7)	30 (71.4)	0.63**
Grade ≥III	8 (10.4)	5 (14.3)	3 (7.1)	0.46**
ICANS no. (%)				0.53
no onset	**76 (69.1)**	**35 (72.9)**	**41 (66.1)**	
onset	**34 (30.9)**	**13 (27.1)**	**21 (33.9)**	
ICANS Grading no. (% of onset)				
Grade I	13 (38.2)	7 (53.8)	6 (28.6)	
Grade II	12 (35.3)	3 (23.1)	9 (42.9)	
Grade III	9 (26.5)	3 (23.1)	6 (28.6)	
Grade IV	0 (0)	0 (0)	0 (0)	
Grade ≥II	21 (61.8)	6 (46.2)	15 (71.4)	0.17**
Grade ≥III	9 (26.5)	3 (23.1)	6 (28.6)	1.0**

Abbreviations: *CH*= clonal hematopoiesis; *CRS*= Cytokine release syndrome *ICANS*= Immune effector cell-associated neurotoxicity syndrome *no.*=number; **Statistics: *)** calculated with Fisher's exact test ****)** calculation within cohort of onset

Supplemental Table 10. CRS and ICANS frequency according to CH with low and high VAF.

Toxicity	A: CH negative n=48	B: CH positive VAF 1-5% n=35	C: CH positive VAF >5% n=27	P-value* A vs B	P-value* A vs C	P-value* B vs C
CRS no. (%)				1.0	0.44	0.59
no onset	**13 (27.1)**	**10 (28.6)**	**10 (37.0)**			
onset	**35 (72.9)**	**25 (71.4)**	**17 (63.0)**			
CRS Grading no. (% of onset)						
Grade I	12 (34.3)	7 (28.0)	5 (29.4)			
Grade II	18 (51.4)	18 (72.0)	9 (52.9)			
Grade III	4 (11.4)	0 (0)	3 (17.6)			
Grade IV	1 (2.9)	0 (0)	0 (0)			
Grade ≥II	23 (65.7)	18 (72.0)	12 (70.6)	0.78**	1.0**	1.0**
Grade ≥III	5 (14.3)	0 (0)	3 (17.6)	0.07**	1.0**	0.06**
ICANS no. (%)				0.16	0.78	0.11
no onset	**35 (72.9)**	**20 (57.1)**	**21 (77.8)**			
onset	**13 (27.1)**	**15 (42.9)**	**6 (22.2)**			
ICANS Grading no. (% of onset)						
Grade I	7 (53.8)	4 (26.7)	2 (33.3)			
Grade II	3 (23.0)	7 (46.7)	2 (33.3)			
Grade III	3 (23.0)	4 (26.7)	2 (33.3)			
Grade IV	0 (0)	0 (0)	0 (0)			
Grade ≥II	6 (46.2)	11 (73.3)	4 (66.7)	0.25**	0.63**	1.0**
Grade ≥III	3 (23.0)	4 (26.7)	2 (33.3)	1.0**	1.0**	1.0**

Abbreviations: *CH*= clonal hematopoiesis; *VAF*= variant allele frequency; *CRS*= Cytokine release syndrome *ICANS*= Immune effector cell-associated neurotoxicity syndrome *no.*=number; **Statistics: *)** calculated with Fisher's exact test ****)** calculation within cohort of onset

Supplemental Table 11. CRS and ICANS Frequency according to age.

	Age<60				Age≥60			
Toxicity	**A: Total Cohort n=42**	**B: CH neg. n=28**	**C: CH pos. n=14**	**P-value* B vs C**	**A: Total Cohort n=68**	**B: CH neg. n=20**	**C: CH pos. n=48**	**P-value* B vs C**
CRS no. (%)				0.72				0.57
no onset	**11 (26.2)**	**8 (28.6)**	**3 (21.4)**		**22 (32.4)**	**5 (25.0)**	**17 (35.4)**	
onset	**31 (73.8)**	**20 (71.4)**	**11 (78.6)**		**46 (67.6)**	**15 (75.0)**	**31 (64.6)**	
CRS Grading no. (% of onset)								
Grade I	10 (32.3)	8 (40.0)	2 (18.2)		14 (30.4)	4 (26.7)	10 (32.3)	
Grade II	18 (58.1)	10 (50.0)	8 (72.7)		27 (58.7)	8 (53.3)	19 (61.3)	
Grade III	3 (9.7)	2 (10.0)	1 (9.1)		4 (8.7)	2 (13.3)	2 (6.5)	
Grade IV	0 (0)	0 (0)	0 (0)		1 (2.2)	1 (6.7)	0 (0)	
Grade ≥II	21 (67.7)	12 (60.0)	9 (81.8)	0.26**	32 (69.6)	11 (73.3)	21 (67.7)	1.0**
Grade ≥III	3 (9.7)	2 (10.9)	1 (9.1)	1.0**	5 (10.9)	3 (20.0)	2 (6.5)	0.31**
ICANS no. (%)				1.0				0.59
no onset	**32 (76.2)**	**21(75.0)**	**11 (78.6)**		**44 (64.7)**	**14 (70.9)**	**30 (62.5)**	
onset	**10 (23.8)**	**7 (25.0)**	**3 (21.4)**		**24 (35.3)**	**6 (30.0)**	**18 (37.5)**	
ICANS Grading no. (% of onset)								
Grade I	9 (90.0)	6 (85.7)	3 (100)		4 (16.7)	1 (16.7)	3 (16.7)	
Grade II	0 (0)	0 (0)	0 (0)		12 (50.0)	3 (50.0)	9 (50.0)	
Grade III	1 (10.0)	1 (14.3)	0 (0)		8 (33.3)	2 (33.3)	6 (33.3)	
Grade IV	0 (0)	0 (0)	0 (0)		0 (0)	0 (0)	0 (0)	
Grade ≥II	1 (10.0)	1 (14.3)	0 (0)	1.0**	20 (83.3)	5 (83.3)	15 (83.3)	1.0**
Grade ≥III	1 (10.0)	1 (14.3)	0 (0)	1.0**	8 (33.3)	2 (33.3)	6 (33.3)	1.0**
CRS Onset general	31 (73.8)				46 (67.6)			0.5
ICANS onset general	10 (23.8)				24 (35.3)			0.29

Abbreviations: *CH*= clonal hematopoiesis; *CRS*= Cytokine release syndrome *ICANS*= Immune effector cell-associated neurotoxicity syndrome *no.*=number; **Statistics: *)** calculated with Fisher's exact test ****)** calculation within cohort of onset

Supplemental Table 12. Tisagenlecleucel and Axicabtagene-Ciloleucel toxicity outcomes according to mutational status.

	Tisagenlecleucel n=56			Axicabtagene-Ciloleucel n=43		
Toxicity	**A: CH neg. n=25**	**B: CH pos. n=31**	**P-value* A vs B**	**A: CH neg. n=19**	**B: CH pos. n=24**	**P-value* A vs B**
CRS no. (%)			0.59			1.0
no onset	**9 (36.0)**	**14 (45.2)**		**3 (15.8)**	**4 (16.7)**	
onset	**16 (64.0)**	**17 (54.8)**		**16 (84.2)**	**20 (83.3)**	
CRS Grading no. (% of onset)						
Grade I	7 (43.8)	4 (23.5)		5 (31.2)	7 (35.0)	
Grade II	8 (50.0)	12 (70.6)		8 (50.0)	12 (60.0)	
Grade III	0 (0)	1 (5.9)		3 (18.8)	1 (5.0)	
Grade IV	1 (6.3)	0 (0)		0 (0)	0 (0)	
Grade ≥II	9 (56.3)	13 (76.5)	0.28**	11 (68.8)	13 (65.0)	1.0**
Grade ≥III	1 (6.3)	1 (4.9)	1.0**	3 (18.8)	1 (5.0)	0.3**
ICANS no. (%)			0.32			0.22
no onset	**19 (76.0)**	**27 (87.1)**		**12 (63.2)**	**10 (41.7)**	
onset	**6 (24.0)**	**4 (12.9)**		**7 (36.8)**	**14 (58.3)**	
ICANS Grading no. (% of onset)						
Grade I	4 (66.7)	1 (25.0)		3 (42.9)	4 (28.6)	
Grade II	1 (16.7)	2 (50.0)		2 (28.6)	5 (35.7)	
Grade III	1 (16.7)	1 (25.0)		2 (28.6)	5 (35.7)	
Grade IV	0 (0)	0 (0)		0 (0)	0 (0)	
Grade ≥II	2 (33.3)	3 (75.0)	0.52**	4 (57.1)	10 (71.4)	0.64**
Grade ≥III	1 (16.7)	1 (25.0)	1.0**	2 (28.6)	5 (35.7)	1.0**

Abbreviations: *CH*= clonal hematopoiesis; *CRS*= Cytokine release syndrome *ICANS*= Immune effector cell-associated neurotoxicity syndrome *vs* =versus *no*.=number; **Statistics: *)** calculated with Fisher's exact test ****)** calculation within cohort of onset

Supplemental Table 13. Toxicity, response, and survival according to DDR mutational status.

Toxicity	**A: CH negative n=48**	**B: CH positive DDR Mutation n=36**	**C: CH positive Other than DDR n=26**	**P-value* A vs B**
CRS - no. (%)				
no onset	**13 (27.1)**	**15 (41.7)**	**5 (19.2)**	
onset	**35 (72.9)**	**21 (58.3)**	**21 (80.8)**	0.17
CRS Grading - no. (% of onset)				
Grade I	12 (34.3)	9 (42.9)	3 (14.3)	
Grade II	18 (51.4)	11 (52.4)	16 (76.2)	
Grade III	4 (11.4)	1 (4.7)	2 (9.5)	
Grade IV	1 (2.9)	0 (0)	0 (0)	
Grade ≥II	23 (65.7)	12 (57.1)	18 (85.7)	**0.57
Grade ≥III	5 (14.3)	1 (4.7)	2 (9.5)	**0.39
ICANS no. (%)				
no onset	**35 (72.9)**	**28 (77.8)**	**13 (50)**	
onset	**13 (27.1)**	**8 (22.2)**	**13 (50)**	0.8
ICANS Grading no. (% of onset)				
Grade I	7 (53.8)	4 (50)	2 (15.4)	
Grade II	3 (23.1)	1 (12.5)	8 (61.5)	
Grade III	3 (23.1)	3 (37.5)	3 (23.1)	
Grade ≥II	6 (46.2)	4 (50)	11 (84.6)	**1.0
Grade ≥III	3 (23.1)	3 (37.5)	3 (23.1)	**0.63
1y-OS	55%	40%	62%	
1y-PFS	46%	25%	51%	
Number of Pat.	**n=45**	**n=35**	**n=25**	
Best Response* no. (% of responder)**	28 (62.2)	26 (74.3)	20 (80)	0.25

Abbreviations: *DDR*= DNA Damage Response (DDR-Group, PPM1D±TP53±CHEK2±ATM); *CH*= clonal hematopoiesis; *CRS*= Cytokine release syndrome *ICANS*= Immune effector cell-associated neurotoxicity syndrome *vs* =versus *no*.=number; **Statistics: *)** calculated with Fisher's exact test ****)** calculation within cohort of onset
*****)** Period of observation d0-d180 after CAR T-cell therapy

Supplemental Table 14. Toxicity, response, and survival according to DTA mutational status.

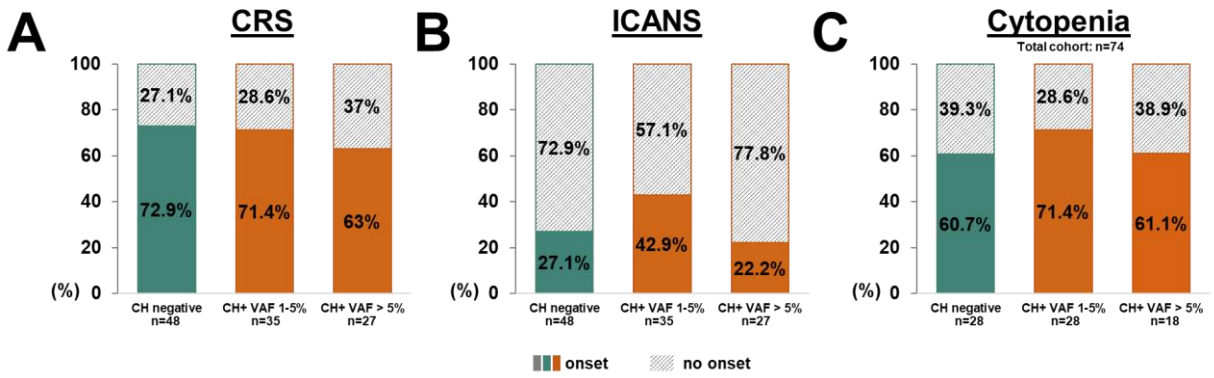
Toxicity	**A: CH negative n=48**	**B: CH positive DTA Mutation n=39**	**C: CH positive Other than DTA n=23**	**P-value* A vs B**
CRS - no. (%)				
no onset	**13 (27.1)**	**15 (38.5)**	**5 (21.7)**	
onset	**35 (72.9)**	**24 (61.5)**	**18 (78.3)**	0.36
CRS Grading - no. (% of onset)				
Grade I	12 (34.3)	4 (16.7)	8 (44.4)	
Grade II	18 (51.4)	17 (70.8)	10 (55.6)	
Grade III	4 (11.4)	3 (12.5)	0 (0)	
Grade IV	1 (2.9)	0 (0)	0 (0)	
Grade ≥II	23 (65.7)	20 (3.3)	10 (55.6)	0.23**
Grade ≥III	5 (14.3)	3 (12.5)	0 (0)	1.0**
ICANS no. (%)				
no onset	**35 (72.9)**	**23 (59.0)**	**18 (78.3)**	
onset	**13 (27.1)**	**16 (41.0)**	**5 (21.7)**	0.18
ICANS Grading no. (% of onset)				
Grade I	7 (53.8)	4 (25.0)	2 (40.0)	
Grade II	3 (23.1)	7 (43.8)	2 (40.0)	
Grade III	3 (23.1)	5 (31.3)	1 (20.0)	
Grade ≥II	6 (46.2)	12 (75.0)	3 (60.0)	0.14**
Grade ≥III	3 (23.1)	5 (31.3)	1 (20.0)	0.70**
1y-OS	55%	68%	31%	
1y-PFS	46%	45%	17%	
Number of Pat.	**n=45**	**n=39**	**n=21**	
Best Response* no. (% of responder)**	28 (62.2)	30 (76.9)	16 (76.2)	0.16

Abbreviations: *DTA*= DNMT3A±TET2±ASXL1 mutated *CH*= clonal hematopoiesis; *CRS*= Cytokine release syndrome *ICANS*= Immune effector cell-associated neurotoxicity syndrome *vs* =versus *no*.=number; **Statistics: *)** calculated with Fisher's exact test ****)** calculation within cohort of onset *****)** Period of observation d0-d180 after CAR T-cell therapy

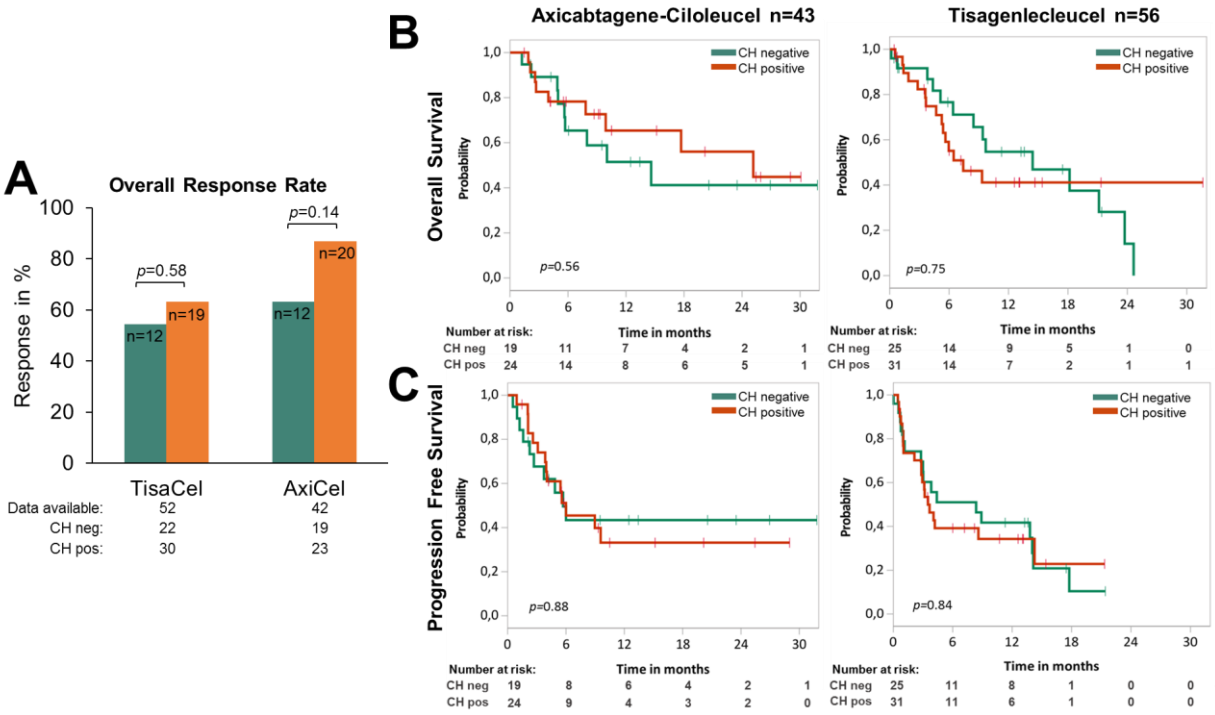
Supplemental Figures

Supplemental Figure 1. Toxicity outcomes according to CH with low (1-5%) and high VAF (>5%).

(A) Histogram plots showing prevalence of CRS (onset: filled, no onset: hatched) according to absence (n=48, green) or presence (orange) of clonal hematopoiesis with low (1-5%) (n=35) and high VAF (>5%) (n=27) across the total cohort. **(B)** Diagrams showing prevalence of ICANS according to absence (n=48) or presence of clonal hematopoiesis with low (1-5%) (n=35) and high VAF (>5%) (n=27) across the total cohort. **(C)** Histogram plots illustrating prevalence of cytopenias at day 100 after CAR T-cell therapy in patients with available information (n=74) according to absence (n=28) or presence of clonal hematopoiesis with low (1-5%) (n=28) and high VAF (>5%) (n=18).

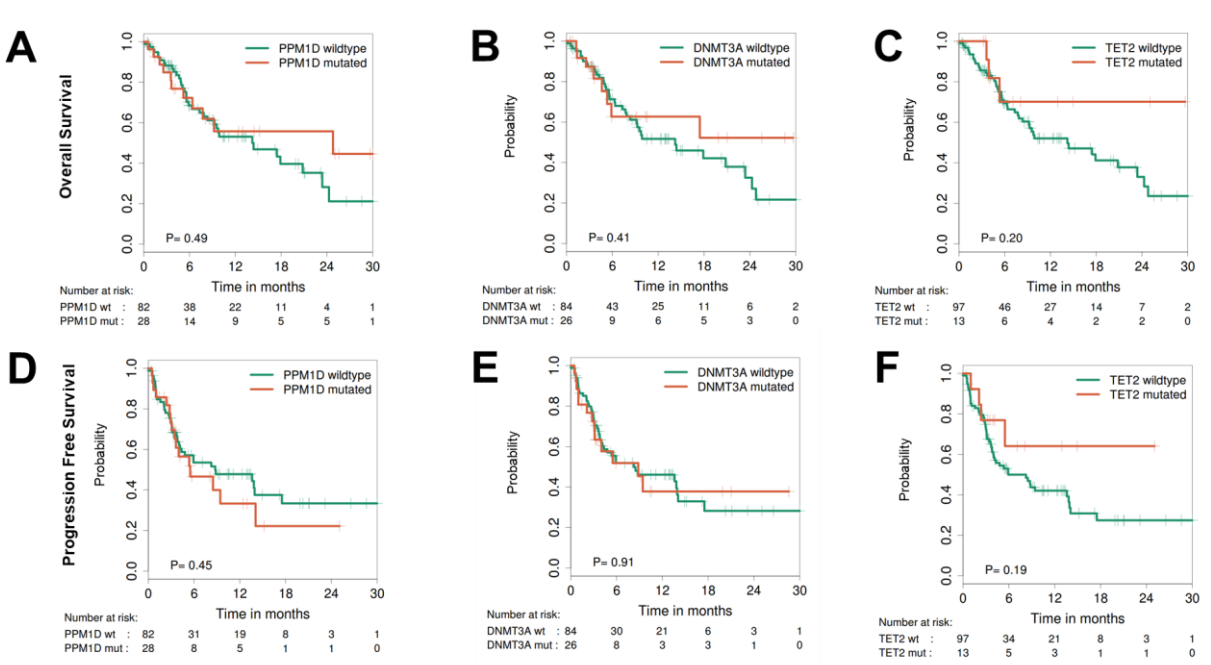


Supplemental Figure 2. Response and survival regarding CAR T-cell construct and mutational status.
(A) Diagram demonstrating the best overall response rate (ORR) in patients treated with Axi-cel (n= 43) or Tisa-cel (n=56) according to mutational status in the first 180 days after Car T-cell treatment. P-value was calculated with Fisher's exact test. Patients with lack of follow-up data or death before progress/response were excluded. **(B)** Kaplan-Meier curves depict the overall survival stratified by absence or presence of clonal hematopoiesis with a VAF cutoff 1% for Axi-cel or Tisa-cel. Cox regression: Axi-cel: 1Y-OS 65% vs. 52%, HR: 0.76, CI: 0.30-1.92; Tisa-cel: 1Y-OS 41% vs. 55%, HR: 1.13, CI: 0.54-2.36; **(C)** Kaplan-Meier curves show progression-free survival stratified by absence or presence of clonal hematopoiesis with a VAF cutoff 1%. Cox regression: Axi-cel:1Y-PFS 33% vs 43%, HR:1.06, CI: 0.47-2.40; Tisa-cel: 1Y-PFS 34% vs 42%, HR:1.07, CI: 0.56-2.06. P-value was calculated for **(B)** and **(C)** with log-Rank test.



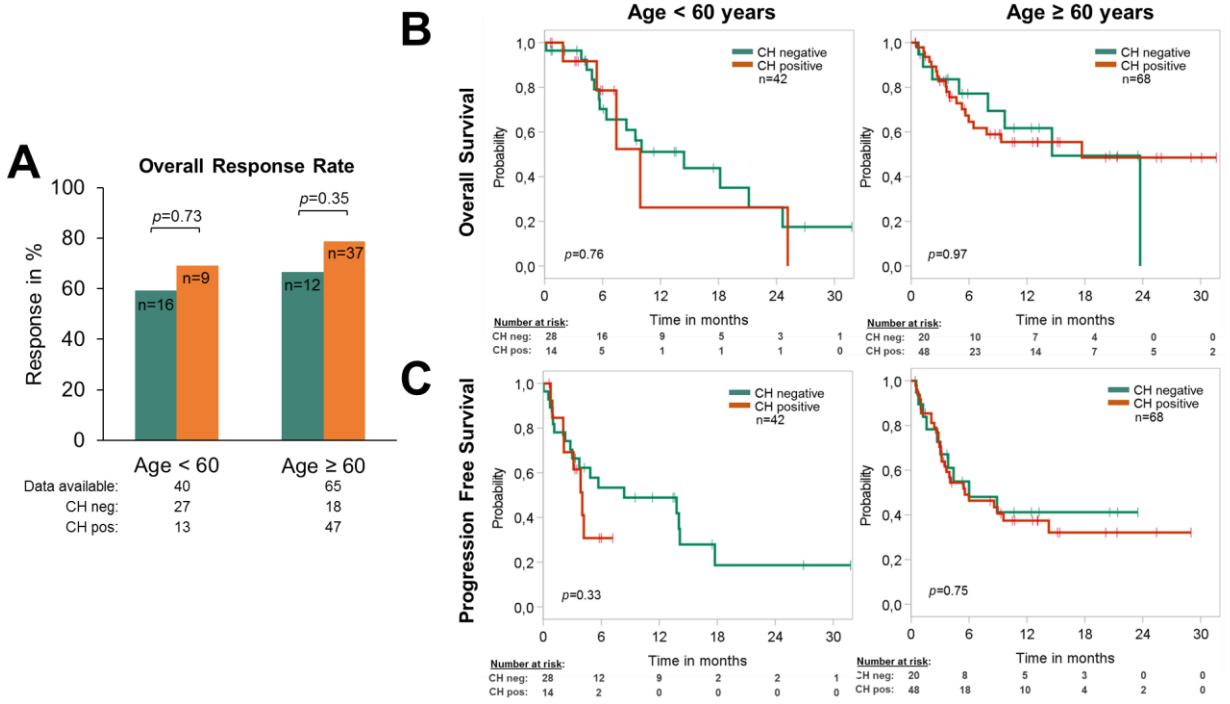
Supplemental Figure 3. OS and PFS by mutational status of *PPM1D, DNMT3A*, and *TET2*.

(A-C) Kaplan-Meier curves depict OS stratified by absence or presence of clonal hematopoiesis with a VAF cutoff 1% in the genes *PPM1D, DNMT3A*, or *TET2*. **(D-F)** Kaplan-Meier curves depict PFS stratified by absence or presence of clonal hematopoiesis with a VAF cutoff 1% in the genes *PPM1D*, *DNMT3A*, or *TET2*. P-value was calculated with the log-Rank test.



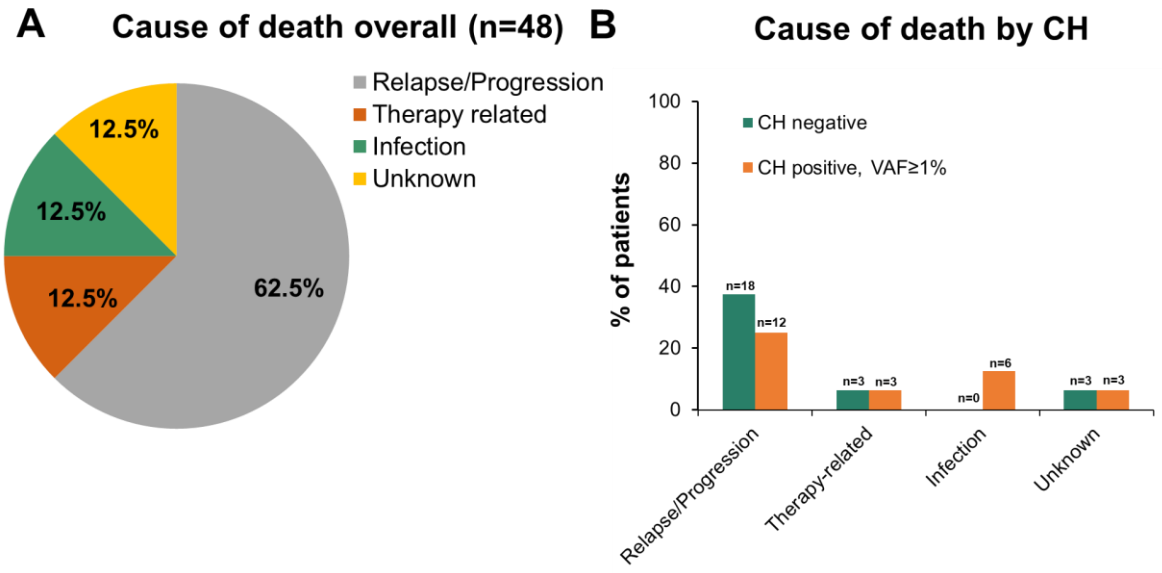
Supplemental Figure 4. Response and survival in patients above/below 60 years of age according to mutational status.

(A) Diagram demonstrating the best overall response rate (ORR) in the first 180 days after Car T-cell treatment within subgroups divided by age above/below 60 years at d0 and stratified by absence or presence of clonal hematopoiesis with a VAF cutoff 1%, respectively. P-value was calculated with Fisher's exact test. Patients with lack of follow-up data or death before progress/response were excluded. **(B)** Kaplan-Meier curves depict the overall survival stratified by absence or presence of clonal hematopoiesis with a VAF cutoff 1% for patients below or above 60 years at treatment day. **(C)** Kaplan-Meier curves show progression-free survival stratified by absence or presence of clonal hematopoiesis with a VAF cutoff 1% for patients below or above 60 years at treatment day. P-value was calculated for **(B)** and **(C)** with the log-Rank test.



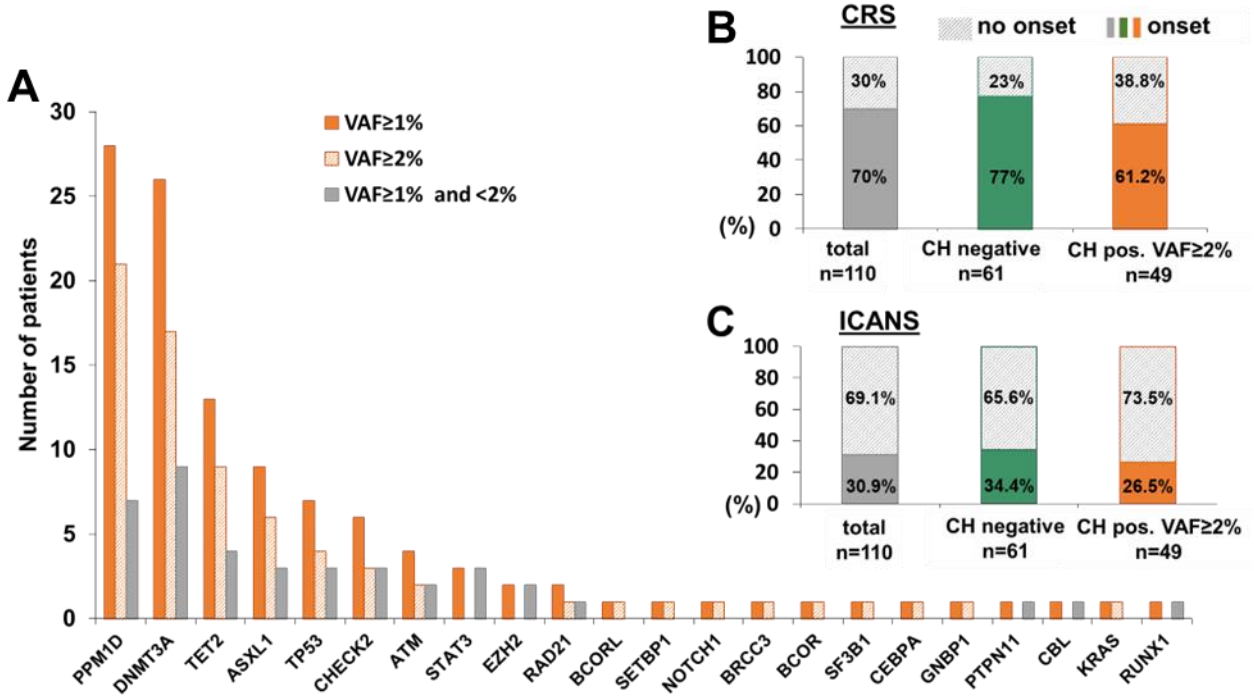
Supplemental Figure 5. Causes of death according to CH using a 1% VAF cutoff.

(A) During the observation time 48 patients died. The frequency of different causes of death are shown for all deceased patients. **(B)** The percentage of patients who deceased from different causes are shown for CH positive and CH negative patients. The absolute number of patients is shown in the figure.



Supplemental Figure 6. Toxicity outcomes according to CH using a 2% VAF cutoff.

(A) Frequency of CH across the entire cohort (n=110) as measured by the VAF using a cutoff of 2%. **(B)** Prevalence of CRS according to absence or presence of CH using a 2% VAF cutoff. **(C)** Prevalence of ICANS according to absence or presence of CH using a 2% VAF cutoff.



Supplemental Figure 7. Response and survival according to CH using a 2% VAF cutoff.

(A) Best overall response rate (ORR) during the first 180 days after CAR T-cell treatment stratified by absence (green, n=58) or presence (orange, n=47) of CH with a VAF cutoff of 2%. P-value was calculated with Fisher's exact test. Patients with lack of follow-up data or death before progression/response were excluded (n=5). **(B)** Kaplan-Meier curves showing OS of 110 patients undergoing CAR T-cell therapy stratified by absence (green, n=61) or presence (orange, n=49) of CH with a VAF cutoff of 2%. **(C)** Kaplan-Meier curves showing progression-free survival of 110 patients undergoing CAR T-cell therapy stratified by absence (green, n=61) or presence (orange, n=49) of CH with a VAF cutoff of 2%. P-value was calculated for (B) and (C) with log-Rank test.