Lenalidomide results in a durable complete remission in acute myeloid leukemia accompanied by persistence of somatic mutations and a T-cell infiltrate in the bone marrow

Dhruv Bansal,[1] Kiran Vij,[1] Gue Su Chang,[2] Christopher A. Miller,[2] John F. DiPersio,[1] Ravi Vij,[1] Sharon E. Heath,[1] Peter Westervelt,[1] John S. Welch[1] and Todd A. Fehniger[1*]*

[1]Department of Medicine, Division of Oncology, BMT and Leukemia Program, Washington University School of Medicine, Saint Louis, MO and [2]McDonnell Genome Institute, Washington University School of Medicine, Saint Louis, MO, USA

**JSW and TAF contributed equally to this work*

Correspondence: tfehnige@wustl.edu/jwelch@wustl.edu
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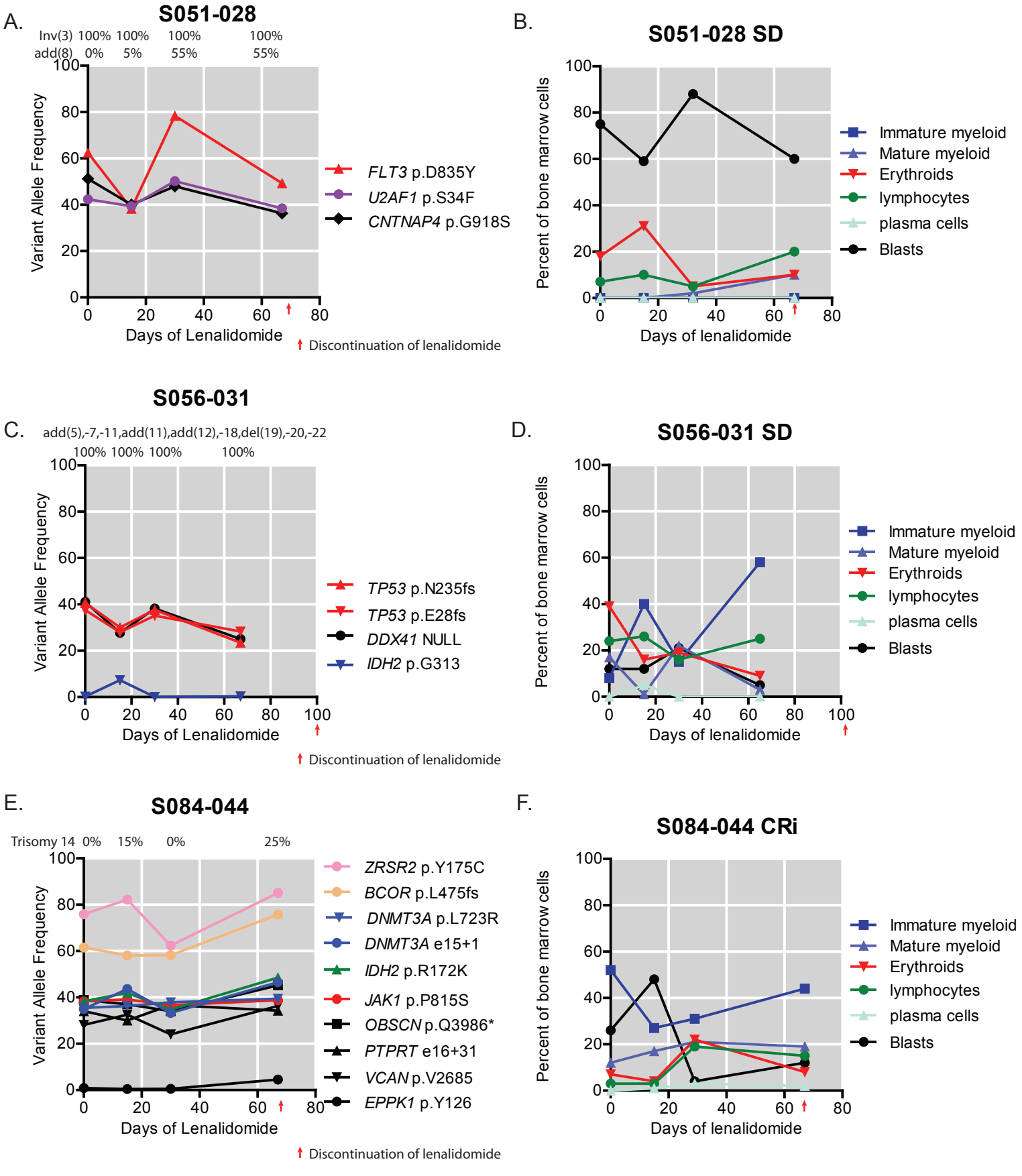

Supplemental Figure 1. Mutations and morphology in three additional cases.

Supplemental Table 1. Mutations detected in patient S058-034

Chr	start	stop	ref	var	type	Gene	Mutation type	Position	Amino acid change	Ensembl gene ID	Tier	Samples mutation was detected	normal VAF	baseline VAF	c1d15 VAF	c2d01 VAF	c2d30 VAF	c6d01 VAF	c8d01 VAF	c14d01 VAF	c12d01 VAF
11	3740671	3740671	T	C	SNP	NUP98	silent	c.2370	p.Q790	ENSG00000110713	tier1	baseline	0.00	14.63	5.66	0.00	0.00	0.00	0.00	0.00	0.00
12	25398285	25398285	C	G	DNP	KRAS	missense	c.34	p.G12R	ENSG00000133703	tier1	c14d01, c8d01, c12d01, c2d01, c6d01	0.87	2.42	3.31	5.71	2.48	17.79	16.50	20.33	14.15
17	51900869	51900869	C	G	SNP	KIF2B	missense	c.475	p.Q159E	ENSG00000141200	tier1	baseline, c14d01, c2d30, c8d01, c12d01, c2d01, c6d01	3.75	33.33	15.28	14.75	19.94	18.51	26.58	26.34	17.17
17	51901046	51901046	G	A	SNP	KIF2B	missense	c.652	p.V218M	ENSG00000141200	tier1	baseline, c1d15, c2d30, c2d01	0.72	25.39	7.72	7.06	10.62	0.24	0.33	1.41	0.36
17	74732959	74732959	G	A	SNP	SRSF2	missense	c.284	p.P95L	ENSG00000161547	tier1	baseline, c14d01, c2d30, c8d01, c12d01, c2d01, c6d01	2.98	32.06	16.38	16.46	22.40	19.91	23.61	23.52	21.14
3	39228131	39228131	C	T	SNP	XIRP1	missense	c.2806	p.G936R	ENSG00000168334	tier1	baseline, c6d01	5.21	39.86	16.26	15.88	26.68	26.03	22.75	30.38	21.19
4	1.06E+08	1.06E+08	C	A	SNP	TET2	nonsense	c.1311	p.Y437*	ENSG00000168769	tier1	baseline, c14d01, c2d30, c8d01, c12d01, c2d01, c6d01	6.05	68.57	29.41	26.63	45.32	48.50	41.55	47.41	31.40
6	33630430	33630430	C	T	SNP	ITPR3	silent	c.837	p.S279	ENSG00000096433	tier1	baseline, c14d01, c1d15, c2d30, c8d01, c12d01, c2d01, c6d01	3.61	29.56	18.92	17.07	23.79	24.77	23.97	27.65	17.75
8	1.18E+08	1.18E+08	T	-	DEL	RAD21	frame_shift	c.1635	p.G547fs	ENSG00000164754	tier1	baseline, c14d01, c2d30, c8d01, c12d01, c2d01, c6d01	4.55	35.33	14.17	24.38	29.00	23.11	24.64	19.03	21.48
X	48652199	48652199	G	C	SNP	GATA1	splice_site	c.871-1	e5-1	ENSG00000102145	tier1	baseline	0.00	23.59	1.55	0.29	0.36	0.00	0.00	0.00	0.49

Supplemental Table 2: Mutation Summary

Patient ID	DEL	INS	SNP	DNP	sum	tier1	tier2	tier3	tier4
S046-025	0	2	4	0	6	5	0	1	0
S051-028	0	0	3	0	3	3	0	0	0
S056-031	0	2	2	0	4	3	1	0	1
S058-034	1	0	8	1	10	10	0	0	0
S063-035	1	0	5	0	6	6	0	0	1
S084-044	1	0	9	0	10	10	0	0	0

Supplemental Table 3. Baseline mutations

Patient ID	Response	Chr	Start	Stop	Ref	Var	Type	Gene	Transcript	Mutation type	Position	Amino acid change	Tier	Samples mutation was detected	Normal reference counts	Normal variant counts	Normal VAF	Baseline reference counts	Basline variant counts	Baseline VAF
S046-025	CRc	2	25467143	25467143	C	A	SNP	DNMT3A	ENST00000264709	nonsense	c.1732	p.E578*	tier1	baseline,C1D15,C6D01	321	5	1.53	290	176	37.61
S046-025	CRc	4	54364887	54364887	T	C	SNP	LNX1	ENST00000263925	missense	c.899	p.H300R	tier1	baseline,C1D15	164	0	0.00	184	55	22.92
S046-025	CRc	11	32417945	32417946	-	CGCGGATGTTTTACCGGGGATTCGGGCGGGACC	INS	WT1	ENST00000332351	frame_shift_ins	c.1107_1106	p.R370fs	tier1	baseline,C1D15	185	0	0.00	233	53	18.53
S046-025	CRc	11	32417947	32417948	-	GACC	INS	WT1	ENST00000332351	frame_shift_ins	c.1105_1104	p.R368fs	tier1	baseline,C1D15	182	0	0.00	218	79	26.60
S046-025	CRc	12	1.18E+08	1.18E+08	C	T	SNP	KSR2	ENST00000339824	intronic	c.1171+16	e5+16	tier3	baseline,C1D15,C2D01,	163	4	2.40	125	79	38.54
S046-025	CRc	17	1563289	1563289	C	T	SNP	PRPF8	ENST00000304992	missense	c.4792	p.D1598N	tier1	C6D01	159	2	1.24	116	57	32.76
S051-028	SD	13	28592642	28592642	C	A	SNP	FLT3	ENST00000380982	missense	c.2503	p.D835Y	tier1	baseline,C1D15,C1D30, C2D30	134	5	3.60	59	98	62.42
S051-028	SD	16	76556154	76556154	G	A	SNP	CNTNAP4	ENST00000307431	missense	c.2752	p.G918S	tier1	baseline,C1D15,C1D30, C2D30	179	14	7.22	146	153	51.17
S051-028	SD	21	44524456	44524456	G	A	SNP	U2AF1	ENST00000291552	missense	c.101	p.S34F	tier1	baseline,C1D15,C1D30, C2D30	112	7	5.79	98	72	42.35
S056-031	SD	5	1.77E+08	1.77E+08	T	C	SNP	DDX41	ENST00000513562	5_prime_untranslated	c.-176941913	NULL	tier2	baseline,C1D15,C1D30, C2D30	258	0	0.00	362	252	41.04
S056-031	SD	15	90630372	90630372	T	G	SNP	IDH2	ENST00000330062	silent	c.939	p.G313	tier1	C1D15	248	0	0.00	546	1	0.18
S056-031	SD	17	7577576	7577577	-	T	INS	TP53	ENST00000269305	frame_shift_ins	c.705_704	p.N235fs	tier1	baseline,C1D15,C1D30, C2D30	162	0	0.00	266	182	40.62
S056-031	SD	17	7579713	7579714	-	CA	INS	TP53	ENST00000269305	frame_shift_ins	c.83_82	p.E28fs	tier1	baseline,C1D15,C1D30, C2D30	89	0	0.00	130	78	37.50
S058-034	CRi	3	39228131	39228131	C	T	SNP	XIRP1	ENST00000340369	missense	c.2806	p.G936R	tier1	baseline,C6D01	563	31	5.21	177	118	39.86
S058-034	CRi	4	1.06E+08	1.06E+08	C	A	SNP	TET2	ENST00000380013	nonsense	c.1311	p.Y437*	tier1	baseline,C14D01,C2D30,C8D01,C12D01,C2D01,C6D01	404	26	6.05	55	120	68.57
S058-034	CRi	6	33630430	33630430	C	T	SNP	ITPR3	ENST00000374316	silent	c.837	p.S279	tier1	baseline,C1D15,C2D30,C8D01,C12D01,C2D01,C6D01	507	19	3.61	143	60	29.56
S058-034	CRi	8	1.18E+08	1.18E+08	T	-	DEL	RAD21	ENST00000297338	frame_shift_del	c.1635	p.G547fs	tier1	baseline,C14D01,C2D30,C8D01,C12D01,C2D01,C6D01	273	13	4.55	97	53	35.33
S058-034	CRi	11	3740671	3740671	T	C	SNP	NUP98	ENST00000324932	silent	c.2370	p.Q790	tier1	baseline	132	0	0.00	70	12	14.63
S058-034	CRi	12	25398285	25398285	C	G	SNP	KRAS	ENST00000256078	missense	c.34	p.G12R	tier1	C14D01,C8D01,C12D01,C2D01,C6D01	229	2	0.87	121	3	2.42
S058-034	CRi	17	51900869	51900869	C	G	SNP	KIF2B	ENST00000268919	missense	c.475	p.Q159E	tier1	baseline,C14D01,C2D30,C8D01,C12D01,C2D01,C6D01	560	22	3.75	175	88	33.33
S058-034	CRi	17	51901046	51901046	G	A	SNP	KIF2B	ENST00000268919	missense	c.652	p.V218M	tier1	baseline,C1D15,C2D30, C2D01	554	4	0.72	191	65	25.39
S058-034	CRi	17	74732959	74732959	G	A	SNP	SRSF2	ENST00000359995	missense	c.284	p.P95L	tier1	baseline,C14D01,C2D30,C8D01,C12D01,C2D01,C6D01	812	25	2.98	283	134	32.06
S058-034	CRi	X	48652199	48652199	G	C	SNP	GATA1	ENST00000376670	splice_site	c.871-1	e5-1	tier1	baseline	423	0	0.00	148	46	23.59
S063-035	SD	5	1.4E+08	1.4E+08	C	A	SNP	PCDHB1	ENST00000306549	silent	c.1764	p.T588	tier1	baseline,C1D15,C2D30	183	3	1.60	252	139	35.55
S063-035	SD	13	28592635	28592637	ATG	-	DEL	FLT3	ENST00000380982	in_frame_del	c.2510_2508	p.I836in_frame_	tier1	C2D30	97	0	0.00	256	2	0.78
S063-035	SD	15	90631934	90631934	C	T	SNP	IDH2	ENST00000330062	missense	c.419	p.R140Q	tier1	baseline,C2D30	166	10	5.68	251	121	32.44
S063-035	SD	17	74732959	74732959	G	T	SNP	SRSF2	ENST00000359995	missense	c.284	p.P95H	tier1	baseline,C1D15,C2D30	278	5	1.77	444	240	35.09
S063-035	SD	20	31024758	31024758	C	T	SNP	ASXL1	ENST00000375687	nonsense	c.4243	p.R1415*	tier1	baseline,C1D15,C1D30, C2D30	224	3	1.32	281	135	32.45
S063-035	SD	21	36231877	36231877	T	G	SNP	RUNX1	ENST00000300305	splice_site	c.509-2	e5-2	tier1	baseline,C1D15,C1D30, C2D30	86	1	1.15	122	104	46.02
S084-044	CRi	1	65307245	65307245	G	A	SNP	JAK1	ENST00000342505	missense	c.2443	p.P815S	tier1	baseline,C1D15,C1D30, C2D30	399	7	1.72	296	184	38.25
S084-044	CRi	1	2.28E+08	2.28E+08	C	T	SNP	OBSCN	ENST00000422127	nonsense	c.11956	p.Q3986*	tier1	baseline,C1D15,C1D30, C2D30	581	4	0.68	435	277	38.90
S084-044	CRi	2	25463514	25463514	A	C	SNP	DNMT3A	ENST00000264709	missense	c.2168	p.L723R	tier1	baseline,C1D15,C1D30, C2D30	329	3	0.90	282	155	35.47
S084-044	CRi	2	25466766	25466766	C	T	SNP	DNMT3A	ENST00000264709	splice_site	c.1936+1	e15+1	tier1	baseline,C1D15,C1D30, C2D30	242	2	0.82	177	95	34.93
S084-044	CRi	5	82836877	82836877	T	G	SNP	VCAN	ENST00000265077	silent	c.8055	p.V2685	tier1	baseline,C1D15,C1D30, C2D30	251	2	0.79	222	87	28.16
S084-044	CRi	8	1.45E+08	1.45E+08	G	A	SNP	EPPK1	ENST00000525985	silent	c.378	p.Y126	tier1	C2D30	470	0	0.00	592	5	0.84
S084-044	CRi	15	90631838	90631838	C	T	SNP	IDH2	ENST00000330062	missense	c.515	p.R172K	tier1	baseline,C1D15,C1D30, C2D30	451	14	3.01	357	222	38.28

S084-044	CRi	20	40864838	40864838	G	A	SNP	PTPRT	ENST00000373198	intronic	c.2399+31	e16+31	tier3	baseline,C1D15,C1D30, C2D30	190	3	1.55	161	83	34.02
S084-044	CRi	X	15827408	15827408	A	G	SNP	ZRSR2	ENST00000307771	missense	c.524	p.Y175C	tier1	baseline,C1D15,C1D30, C2D30	135	8	5.59	40	129	75.88
S084-044	CRi	X	39933177	39933177	G	-	DEL	BCOR	ENST00000378444	frame_shift_del	c.1422	p.L475fs	tier1	baseline,C1D15,C1D30, C2D30	178	3	1.66	92	147	61.51

Supplemental Table 4. Predicted mutation-associated peptides that bind to patient-specific MHCI complexes

Patient ID	Gene Name	Median Mutant Score	Median Wild Type Score	Fold Change
S046-025	LNX1	162	177	1.09
	WT1	452	Insertion, no comparable WT peptide	NA
S051-028	FLT3	12	143	11.86
S056-031	TP53	81	Frame shift, no comparable WT peptide	NA
	TP53	325	20403	62.87
S058-034	No HLA genotyping avalible			
S063-035	No neo-epitopes identified			
S084-044	No neo-epitopes identified			