Clonal hematopoiesis is associated with increased risk of progression of asymptomatic Waldenström Macroglobulinemia.

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SUPPLEMENTARY APPENDIX

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SUPPLEMENTARY METHODS

Statistical analysis

CH was defined as the presence of *DNMT3A*, *TET2* and *ASXL1* mutations (CH-DTA) with a variant allele frequency (VAF) of ≥2%. The average depth of coverage for the CH-DTA mutations (TET2, DNMT3A and ASXL1) was 821X. Variant detection on paired peripheral blood and bone marrow samples have been reported to be 100% on this NGS assay[1]. We defined IgM MGUS and SWM patients as those who were asymptomatic and had <10% or >10% lymphoplasmacytic cell involvement in the BM, respectively[2]. Bone marrow biopsies and aspirates were examined at NGS and the presence of or absence of dysplasia was assessed at that time. Clinical progression was defined by meeting criteria for initiation of therapy according to the recommendations of the 2nd International Workshop for Waldenstrom Macroglobulinemia[2]. Progression-free survival (PFS) was defined as time from diagnosis of MGUS or SWM to progression or death, while OS was defined as time from diagnosis to death from any cause; events were censored at last follow-up date. Survival distributions were estimated using the Kaplan Meier (KM) method, with variance and 95% confidence intervals (CIs) estimated using Greenwood's formula. Median follow-up time was estimated using inverse KM method. Wilcoxon rank-sum and Fisher's exact tests were used to assess CH association with continuous and categorical variables, respectively. Two-sided p-values <0.05 were considered statistically significant. Statistical analyses were performed in R (v 4.0.0).

References

1. Kluk MJ, Lindsley RC, Aster JC, et al. Validation and Implementation of a Custom Next-Generation Sequencing Clinical Assay for Hematologic Malignancies. *J Mol Diagn*. 2016;18(4):507-515.
2. Kyle RA, Treon SP, Alexanian R, et al. Prognostic markers and criteria to initiate therapy in Waldenstrom's macroglobulinemia: consensus panel recommendations from the Second International Workshop on Waldenstrom's Macroglobulinemia. *Semin Oncol*. 2003;30(2):116-120.

SUPPLEMENTARY TABLES

Table S1. List of genes and exons targeted by the clinical NGS assay. The NGS assay has three versions that were developed over time and version 2 and 3 were used in this cohort. (A) Version 2 (n=574). (B) Version 3 (n=59)

A

Gene	Exon	Gene	Exon
ABL1	e2-e10	MAP2K1	e2-e3
ASXL1	e1-e13	MEF2B	e3
ATM	e2-e63	MPL	e10
BCL11B	e4	MYD88	e5
BCOR	e2-e15	NOTCH1	e24-e28
BCORL1	e1-e12	NOTCH1	e34
BRAF	e15	NOTCH2	e24-e28
BRCC3	e3-e11	NOTCH2	e34
CALR	e9	NOTCH3	e25-e26
CBL	e7-e8	NOTCH3	e33
CBLB	e9-e11	NPM1	e10-e11
CD79B	e5-e6	NRAS	e2-e5
CEBPA	e1	PAX5	e3 e6-e7
CNOT3	e1-e2	NT5C2	e9, e11, e13, e15, e17
CREBBP	e2-e21, e23-31	PDS5B	e3-e35
CRLF2	e6	PHF6	e2-e10
CSF1R	e22	PDGFRA	e10-e21, e23
CSF3R	e14-e18	PIGA	e2-e6
CTCF	e3-e12	PIM1	e1-e6
CTNNB1	e2-e4	PRPF40B	e2-e26
CUX1	e1-e21	PIK3CA	e2, e10, e21
CXCR4	e2	PRPF8	e2-e43
DNMT3A	e2-e23	PTEN	e1-e9
DNMT3B	e2-e23	PTPN11	e1-e15
EED	e1-e12	RAD21	e2-e14
EGFR	e18-e21	RET	e7
EP300	e18-e27	RIT1	e1-e6
ETV6	e1-e8	RPL10	e5
FANCL	e1-e14	RUNX1	e2-e9
FBXW7	e8-e12	SETBP1	e4
EZH2	e2-e8, e11-e20	SF3B1	e12-e16
FLT3	e14-e16, e20	SF1	e1-e10, e13
GATA1	e2-e6	SF3A1	e1-e2, e5-e16
GATA2	e2-e6	SETD2	e1-e4, e6-e21
		SH2B3	e2-e8
GATA3	e4-e6	SMC1A	e1-e25
GNAS	e8-e9	SMC3	e2-e29
GNB1	e5-e6	SRSF2	e1
IDH1	e4	STAG2	e3-e35
IDH2	e4	TET2	e3-e11

IKZF1	e2-e8	STAT3	e2-e17, e21-23
IKZF2	e1-e8	TLR2	e1
IKZF3	e1-e8	TP53	e2-e11
IL7R	e6	U2AF1	e2, e6
JAK1	e10-e25	U2AF2	e1-e12
JAK2	e12, e14	WHSC1	e17-e18
JAK3	e11-e24	WT1	e1-e10
KIT	e8-9, e11, e17	XPO1	e15-e16
KRAS	e2-e5	ZRSR2	e1-e11
LUC7L2	e3-e11		

B

Gene	**Exon**	**Gene**	**Exon**
ABL1	e1-e10	KIT	e8-e11, e17
ASXL1	e11-e12	KRAS	e1-e5
ATM	e1-e62	KMT2A	partial
ATRX	e1-e35	MAP2K1	e2-e3, e6
BCOR	e1-e14	MPL	e4, e10
BCORL1	e1-e13	NF1	e1-e58
BRAF	e11-e15	MYC	e1-e3
BRCC3	e1-e11	MYD88	e5
BTK	e1, e15-e16	NOTCH2	e24-e28, e34
CALR	e9	NFE2	e3-e4
CBL	e7-e9	NOTCH1	e24-e28, e34
CCND1	e1-e5	NSD2	e18-e19
CD79B	e5-e6	NPM1	e10-e11
CDKN2A	e1-e5	NRAS	e1-e4
CDKN2B	e1-e2	PIGA	e1-e62
CEBPA	e1	NT5C2	e12-e20
CREBBP	e1-e31	PHF6	e1-e9
CRLF2	e6	PRPF8	e25-e34
CSF3R	e12-e16	PLCG2	e19-e20, e24
CSNK1A1	e1-e11	PPM1D	e6, e27, e30
CTCF	e1-e10	RAD21	e1-e13
CUX1	e1-e34	PTEN	e1-e9
CXCR4	e3	PTPN11	e1-e15
DDX41	e1-e17	SBDS	e1-e5
DKC1	e1-e15	RIT1	e1-e6
DNMT3A	e1-e25	RUNX1	e1-e9
EP300	e1-e31	SF3B1	e12-e18
ERG	e1-e12	SETBP1	e4
ETNK1	e3	SETD2	e1-e21
ETV6	e1-e8	SMC3	e1-e29
EZH2	e1-e19	SH2B3	e1-e8
FBXW7	e8-e12	SMC1A	e1-e26
FLT3	e14,e16-e17,e20	STAT3	e2-e24
GATA1	e1-e5	SRSF2	e1
GATA2	e1-e5	STAG2	e1-e33

GNAS	e8-e9	TERT	e1-e16
GNB1	e5-e6	STAT5B	e13-e19
IDH1	e3-e10	TERC	e1
IDH2	e1-e11	U2AF1	e2,e6
IKZF1	e1-e9	TET2	e1-e9
IL7R	e5-e7	TP53	e1-e12
JAK1	e10-e25	ZRSR2	e1-e11
JAK2	e12-e20	WT1	e1-e11
JAK3	e16-e24	XPO1	e15-e16

Table S2. List of called genes and variants at time of NGS assay.

Gene	Chromosome	Variant Classification	Variant Type	Reference Allele	Alternative Allele	cDNA Change	Protein Change	Total Depth	Variant Allele Frequency	NGS Panel Version	Sample ID
ASXL1	20	Frameshift	INS	A	AG	c.1926_1927insG	G642fs*	221	81.45	2	165
ASXL1	20	Frameshift	INS	A	AG	c.1926_1927insG	G642fs*	335	52.24	2	136
ASXL1	20	Frameshift	INS	A	AG	c.3168_3169insG	T1056fs*	1307	45.98	2	511
ASXL1	20	Frameshift	INS	A	AG	c.1926_1927insG	G642fs*	464	39.01	2	947
ASXL1	20	Nonsense	SNP	C	T	c.2332C>T	Q778*	1623	35.49	2	856
ASXL1	20	Frameshift	INS	A	AG	c.1926_1927insG	G642fs*	410	23.9	2	471
ASXL1	20	Nonsense	SNP	C	T	c.2077C>T	R693*	202	22.77	2	1014
ASXL1	20	Frameshift	DEL	GCT	G	c.1475_1476delCT	A492fs*	739	22.19	2	1557
ASXL1	20	Frameshift	DEL	TCACCACTGCCATAGAGAGGCGGC	T	c.1888_1910delCACCACTGCCATAGAGAGGCGGC	G629fs*	144	20.14	2	1701
ASXL1	20	Frameshift	DEL	TCACCACTGCCATAGAGAGGCGGC	T	c.1888_1910delCACCACTGCCATAGAGAGGCGGC	G629fs*	1028	14.88	2	930
ASXL1	20	Frameshift	INS	A	AG	c.1926_1927insG	G642fs*	383	14.62	2	414
ASXL1	20	Frameshift	INS	A	AG	c.1926_1927insG	p.G646Wfs*12	404	11.88	3	1787
ASXL1	20	Frameshift	DEL	AG	A	c.1927delG	G642fs*	125	8.8	2	552
ASXL1	20	Nonsense	SNP	A	T	c.2641A>T	R881*	2370	8.23	2	779
ASXL1	20	Frameshift	INS	A	AG	c.1926_1927insG	p.G646Wfs*12	867	4.84	3	1498
ASXL1	20	Frameshift	INS	C	CA	c.1275_1276insA	Y425fs*	372	4.3	2	268
ASXL1	20	Nonsense	SNP	C	T	c.2644C>T	Q882*	1803	2.05	2	1133
ATM	11	Nonsense	SNP	C	T	c.8197C>T	Q2733*	1248	17.31	2	1041
ATM	11	Frameshift	INS	T	TA	c.5706_5707insA	p.S1905Ifs*25	832	4.33	3	252
ATRX	X	Frameshift	DEL	CT	C	c.3210delA	p.G1071Efs*47	291	43.64	3	1702
BCOR	X	Nonsense	SNP	G	A	c.2428C>T	R810*	230	45.22	2	338
BCOR	X	Frameshift	DEL	CCCTTCCGGAG	C	c.1197_1206delCCTTCCGGAG	G400fs*	499	13.43	2	43
BCOR	X	Frameshift	INS	G	GT	c.2020_2020insA	L673fs*	943	8.06	2	1521
BCOR	X	Frameshift	DEL	CA	C	c.4636delT	I1545fs*	600	6.67	2	909
BCORL1	X	Deletion	DEL	CAGA	C	c.3756_3758delAGA	Deletion	308	93.51	2	1332
BCORL1	X	Frameshift	DEL	AG	A	c.4697delG	E1566fs*	310	4.52	2	243
BRAF	7	Missense	SNP	A	T	c.1790T>A	L597Q	587	14.99	2	427
BRAF	7	Missense	SNP	T	C	c.1801A>G	K601E	584	9.08	2	427
BRCC3	X	Nonsense	SNP	C	T	c.823C>T	Q275*	142	42.96	2	511
CALR	19	Deletion	DEL	AGAG	A	c.1132_1134delGAG	E378del	39	48.72	2	1358
CALR	19	Deletion	DEL	TGAG	T	c.1192_1194delGAG	Deletion	50	36	2	1106
CALR	19	Deletion	DEL	TGAGGATGAG	T	c.1177_1185delGAGGATGAG	392_394delEDE	224	25.45	2	655
CBL	11	Missense	SNP	G	A	c.1259G>A	R420Q	135	41.48	2	1014
CBL	11	Missense	SNP	G	A	c.1211G>A	C404Y	427	24.59	2	511
CBL	11	Missense	SNP	A	T	c.1112A>T	Y371F	590	4.41	2	155
CBL	11	Missense	SNP	T	C	c.1139T>C	L380P	1261	3.09	2	933
CD79B	17	Missense	SNP	T	C	c.590A>G	Y197C	360	26.94	2	1297
CD79B	17	Missense	SNP	A	G	c.589T>C	Y197H	247	10.53	2	1110
CD79B	17	Missense	SNP	A	G	c.589T>C	Y197H	357	6.44	2	1333
CD79B	17	Missense	SNP	T	C	c.590A>G	Y197C	283	6.01	2	527
CD79B	17	Missense	SNP	T	C	c.590A>G	p.Y197C	1648	4.13	3	696

CD79B	17	Missense	SNP	T	G	c.590A>C	Y197S	461	2.82	2	1462
CD79B	17	Missense	SNP	T	C	c.590A>G	Y197C	461	2.82	2	1462
CREBBP	16	Frameshift	DEL	GA	G	c.704delA	S235fs*	17	35.29	2	457
CREBBP	16	Frameshift	DEL	CTTCTAACACATTGGGCCAGAAATCACCT	C	c.4651_4678delAGGTGATTTCTGGCCCAATGTGTTAGAA	E1550fs*	1369	11.25	2	1685
CREBBP	16	Nonsense	SNP	A	T	c.3657T>A	C1219*	444	5.41	2	933
CTCF	16	Missense	SNP	C	A	c.1133C>A	P378Q	127	8.66	2	1331
CXCR4	2	Nonsense	SNP	G	A	c.1000C>T	R334*	532	45.3	2	531
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	571	41.51	2	123
CXCR4	2	Nonsense	SNP	G	T	c.1013C>A	S338*	558	38.17	2	699
CXCR4	2	Nonsense	SNP	G	T	c.1013C>A	S338*	614	34.2	2	1016
CXCR4	2	Frameshift	DEL	CTCAGACT	C	c.1035_1041delAGTCTGA	E346fs*	279	32.97	2	1285
CXCR4	2	Frameshift	INS	A	AT	c.977_977insA	L326fs*	428	31.78	2	621
CXCR4	2	Frameshift	INS	G	GT	c.1008dupA	p.H337Tfs*7	659	30.8	3	459
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	655	29.92	2	1593
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	647	27.51	2	1127
CXCR4	2	Frameshift	INS	A	AG	c.986_986insC	L329fs*	339	24.48	2	389
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	546	23.81	2	1359
CXCR4	2	Nonsense	SNP	C	A	c.1006C>A	G336*	2229	23.69	2	278
CXCR4	2	Frameshift	INS	G	GT	c.953_953insT	T318fs*	625	22.88	2	491
CXCR4	2	Nonsense	SNP	G	T	c.1013C>A	S338*	624	22.12	2	476
CXCR4	2	Nonsense	SNP	G	T	c.1013C>A	S338*	772	21.76	2	1041
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	447	21.7	2	1134
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	493	20.28	2	1350
CXCR4	2	Frameshift	DEL	CA	C	c.1006delT	G335fs*	725	19.59	2	1709
CXCR4	2	Frameshift	DEL	TCG	T	c.1002_1003delCG	R335fs*	710	19.44	2	1709
CXCR4	2	Frameshift	DEL	AATGTC	A	c.1012_1016delGACAT	H337fs*	718	19.08	2	1709
CXCR4	2	Frameshift	INS	G	GT	c.953_953insA	T318fs*	288	18.06	2	1428
CXCR4	2	Frameshift	DEL	AGAGGT	A	c.957_961delACCTC	S320fs*	318	16.98	2	911
CXCR4	2	Frameshift	INS	G	GT	c.953_953insA	T318fs*	275	16.73	2	1451
CXCR4	2	Nonsense	SNP	G	T	c.1013G>T	S338*	1148	15.59	2	152
CXCR4	2	Frameshift	DEL	CAG	C	c.958_959delCT	S319fs*	253	15.42	2	1501
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	588	14.46	2	1024
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	616	14.29	2	1452
CXCR4	2	Nonsense	SNP	G	A	c.1000C>T	R334*	766	13.97	2	1020
CXCR4	2	Frameshift	INS	G	GT	c.953_953insA	T318fs*	317	13.56	2	1556
CXCR4	2	Frameshift	INS	G	GA	c.1012dupT	p.S338Ffs*6	492	13.01	3	1737
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	822	12.53	2	1042
CXCR4	2	Nonsense	SNP	G	T	c.1013C>A	S338*	590	12.37	2	411
CXCR4	2	Nonsense	SNP	G	T	c.1013C>A	S338*	542	12.36	2	1061
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	468	12.18	2	187
CXCR4	2	Frameshift	INS	A	AC	c.1019_1019insG	V340fs*	281	12.1	2	1451

CXCR4	2	Nonsense	SNP	G	A	c.1000C>T	R334*	519	11.75	2	247
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	602	11.63	2	1420
CXCR4	2	Frameshift	DEL	TCA	T	c.961_962delTG	V320fs*	298	11.41	2	1388
CXCR4	2	Nonsense	SNP	G	T	c.1013C>A	S338*	581	11.36	2	527
CXCR4	2	Frameshift	INS	G	GA	c.1022_1022insT	S341fs*	318	11.32	2	1491
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	543	11.23	2	1236
CXCR4	2	Frameshift	INS	A	AGAAG	c.986_986insCTTC	L329fs*	267	10.86	2	1405
CXCR4	2	Frameshift	DEL	ACAGAT	A	c.1019_1023delATCTG	V340fs*	510	10.39	2	1007
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	530	9.62	2	1319
CXCR4	2	Frameshift	INS	G	GA	c.1022_1022insT	S341fs*	302	9.6	2	113
CXCR4	2	Nonsense	SNP	G	A	c.1000C>T	R334*	420	9.52	2	1542
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	p.S338*	530	9.43	3	1769
CXCR4	2	Frameshift	INS	G	GT	c.953_953insA	T318fs*	287	9.41	2	1602
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	534	9.36	2	277
CXCR4	2	Frameshift	DEL	GA	G	c.1022delT	S341fs*	294	8.84	2	430
CXCR4	2	Frameshift	INS	G	GA	c.1022_1022insT	S341fs*	286	8.74	2	1117
CXCR4	2	Nonsense	SNP	G	C	c.1013G>C	S338*	185	8.65	2	32
CXCR4	2	Frameshift	INS	G	GA	c.1022_1022insT	S341fs*	266	8.65	2	599
CXCR4	2	Nonsense	SNP	G	A	c.1000G>A	R334*	1007	8.54	2	978
CXCR4	2	Frameshift	DEL	TGG	T	c.991_992delCC	S330fs*	509	8.45	2	1168
CXCR4	2	Frameshift	DEL	GGA	G	c.1023_1024delTC	S342fs*	311	8.36	2	1429
CXCR4	2	Nonsense	SNP	G	T	c.1013C>A	S338*	555	8.11	2	719
CXCR4	2	Frameshift	INS	G	GA	c.1013_1013insT	S338fs*	447	8.05	2	1478
CXCR4	2	Nonsense	SNP	G	A	c.1000C>T	R334*	577	7.45	2	994
CXCR4	2	Nonsense	SNP	G	A	c.1000G>A	R334*	1449	7.04	2	869
CXCR4	2	Frameshift	INS	C	CT	c.974_974insA	S325fs*	318	6.92	2	1557
CXCR4	2	Nonsense	SNP	G	T	c.1013C>A	S338*	513	6.82	2	399
CXCR4	2	Frameshift	DEL	GAA	G	c.1022_1023delTT	S341fs*	264	6.82	2	760
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	490	6.12	2	1159
CXCR4	2	Nonsense	SNP	G	A	c.1000C>T	R334*	667	6	2	353
CXCR4	2	Frameshift	DEL	AGGTGAGT	A	c.955_961delACTCACC	T318fs*	306	5.88	2	582
CXCR4	2	Nonsense	SNP	G	A	c.1000G>A	R334*	1571	5.86	2	289
CXCR4	2	Nonsense	SNP	G	T	c.1013C>A	S338*	672	5.8	2	715
CXCR4	2	Nonsense	SNP	G	A	c.1000C>T	R334*	506	5.73	2	433
CXCR4	2	Frameshift	INS	A	AC	c.1019_1019insG	V340fs*	285	5.61	2	1691
CXCR4	2	Frameshift	INS	C	CT	c.994_994insA	K331fs*	581	5.34	2	1306
CXCR4	2	Frameshift	INS	G	GA	c.1022_1022insT	S341fs*	281	5.34	2	1118
CXCR4	2	Frameshift	INS	C	CA	c.1018_1018insT	S339fs*	451	5.32	2	517
CXCR4	2	Frameshift	INS	G	GA	c.1013_1013insT	S338fs*	775	5.29	2	933
CXCR4	2	Frameshift	DEL	CA	C	c.1018delT	S339fs*	492	5.28	2	1085
CXCR4	2	Frameshift	INS	C	CA	c.958_958insT	S319fs*	325	5.23	2	569

CXCR4	2	Frameshift	DEL	GA	G	c.1013delT	S338fs*	617	5.19	2	1009
CXCR4	2	Nonsense	SNP	G	A	c.1000C>T	R334*	527	4.93	2	704
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	630	4.92	2	1256
CXCR4	2	Frameshift	DEL	GA	G	c.1013delT	S338fs*	430	4.65	2	1120
CXCR4	2	Nonsense	SNP	G	A	c.1000C>T	R334*	424	4.48	2	1120
CXCR4	2	Frameshift	DEL	GAA	G	c.1020_1021delTT	p.S341Hfs*2	247	4.45	3	1787
CXCR4	2	Nonsense	SNP	G	T	c.1013C>A	S338*	634	4.26	2	394
CXCR4	2	Frameshift	DEL	ATGT	AG	c.1009_1011delinsC	G336fs*	639	4.23	2	1085
CXCR4	2	Nonsense	SNP	G	C	c.1013C>G	S338*	830	4.22	2	201
CXCR4	2	Frameshift	INS	G	GT	c.953_953insA	T318fs*	416	4.09	2	857
CXCR4	2	Frameshift	DEL	ACT	A	c.1030_1031delAG	E343fs*	295	4.07	2	1162
CXCR4	2	Nonsense	SNP	G	A	c.1000C>T	R334*	456	3.95	2	1148
CXCR4	2	Frameshift	DEL	GA	G	c.1013delT	S338fs*	357	3.92	2	1036
CXCR4	2	Nonsense	SNP	T	A	c.991A>T	K331*	695	3.88	2	1005
CXCR4	2	Frameshift	INS	G	GT	c.953_953insT	T318fs*	432	3.7	2	705
CXCR4	2	Frameshift	INS	G	GA	c.1021dupT	p.S341Ffs*3	462	3.68	3	1769
CXCR4	2	Nonsense	SNP	G	T	c.1013C>A	S338*	669	3.44	2	1091
CXCR4	2	Frameshift	DEL			c.1015_1104del	S339fs*	419	3.3	2	128
CXCR4	2	Frameshift	INS	C	CT	c.994_994insA	K331fs*	572	2.97	2	1525
CXCR4	2	Nonsense	SNP	G	A	c.1000C>T	R334*	567	2.65	2	167
CXCR4	2	Frameshift	DEL	TGAAAACTTGAAGACTCAGACTCAGTGGAA	T	c.1049_1077delGAAAACTTGAAGACTCAGACTCAGTGGAA	H350fs*	722	2.63	2	800
CXCR4	2	Frameshift	INS	G	GT	c.952dupA	p.T318Nfs*26	1925	1.04	3	932
DNMT3A	2	Missense	SNP	C	T	c.2312C>T	R771Q	1356	49.63	2	783
DNMT3A	2	Nonsense	SNP	C	T	c.2580G>A	W860*	1165	44.03	2	856
DNMT3A	2	Frameshift	INS	G	GCT	c.883_883insAG	E294fs*	370	42.16	2	338
DNMT3A	2	Missense	SNP	G	A	c.2651C>T	A884V	336	41.07	2	89
DNMT3A	2	Missense	SNP	C	A	c.1628G>T	G543V	273	41.03	2	1155
DNMT3A	2	Frameshift	INS	T	TC	c.1144_1144insG	G381fs*	233	35.62	2	1416
DNMT3A	2	Frameshift	DEL	CA	C	c.1742delT	W581fs*	255	34.51	2	813
DNMT3A	2	Deletion	DEL	AAAG	A	c.2196_2198delCTT	732delF	725	29.79	2	143
DNMT3A	2	Frameshift	DEL	CCACGGCCTTGGCAGTGT	C	c.1198_1214delACACTGCCAAGGCCGTG	V399fs*	643	24.73	2	1347
DNMT3A	2	Missense	SNP	G	A	c.2644C>T	R882C	434	23.27	2	1034
DNMT3A	2	Missense	SNP	A	C	c.2261T>G	L754R	1414	21.92	2	1086
DNMT3A	2	Missense	SNP	A	C	c.929T>G	I310S	895	19.66	2	927
DNMT3A	2	Frameshift	INS	G	GC	c.1762_1762insG	G587fs*	467	19.49	2	857
DNMT3A	2	Frameshift	INS	C	CG	c.700_700insC	P233fs*	292	18.49	2	414
DNMT3A	2	Frameshift	INS	T	TG	c.2008_2008insC	S669fs*	744	18.15	2	900
DNMT3A	2	Frameshift	DEL	GA	G	c.1915delT	S638fs*	258	17.83	2	1438
DNMT3A	2	Frameshift	DEL	TC	T	c.1793delG	p.R598Qfs*53	2037	15.86	3	1768
DNMT3A	2	Nonsense	SNP	C	T	c.939G>A	p.W313*	1664	15.75	3	1787
DNMT3A	2	Missense	SNP	G	A	c.2309G>A	S770L	111	15.32	2	232

DNMT3A	2	Missense	SNP	C	T	c.1945G>A	V649M	377	15.12	2	956
DNMT3A	2	Missense	SNP	A	C	c.2393T>G	L798R	509	14.34	2	956
DNMT3A	2	Frameshift	DEL	GCCCT	G	c.1263_1266delAGGG	G422fs*	338	13.31	2	599
DNMT3A	2	Missense	SNP	C	T	c.2645G>A	R882H	895	13.18	2	28
DNMT3A	2	Frameshift	DEL	AG	A	c.1606delC	S535fs*	339	12.39	2	1346
DNMT3A	2	Frameshift	INS	T	TG	c.1753_1753insC	Y584fs*	224	11.61	2	1120
DNMT3A	2	Missense	SNP	G	A	c.976C>T	R326C	679	11.05	2	1704
DNMT3A	2	Missense	SNP	G	A	c.2644C>T	R882C	768	10.94	2	1008
DNMT3A	2	Missense	SNP	A	G	c.2251T>C	F751L	1619	10.44	2	1063
DNMT3A	2	Frameshift	DEL	CA	C	c.1950delT	L651fs*	350	10.29	2	1341
DNMT3A	2	Missense	SNP	G	A	c.2245C>T	R749C	1362	10.28	2	178
DNMT3A	2	Missense	SNP	G	C	c.2317C>G	p.L773V	1470	10.2	3	1751
DNMT3A	2	Missense	SNP	C	G	c.1628G>C	G543A	337	9.5	2	1623
DNMT3A	2	Missense	SNP	C	A	c.1481G>T	C494F	463	9.29	2	571
DNMT3A	2	Frameshift	DEL	CG	C	c.2375delC	R792fs*	491	8.96	2	1129
DNMT3A	2	Frameshift	DEL	CCA	C	c.2458_2459delTG	L819fs*	295	8.47	2	69
DNMT3A	2	Missense	SNP	C	A	c.1969G>T	V657L	529	7.18	2	139
DNMT3A	2	Frameshift	DEL	AC	A	c.1907delG	V636fs*	549	6.56	2	113
DNMT3A	2	Missense	SNP	C	T	c.977C>T	R326H	894	6.49	2	727
DNMT3A	2	Missense	SNP	G	C	c.2141C>G	S714C	933	6.43	2	1331
DNMT3A	2	Missense	SNP	G	A	c.1903G>A	R635W	931	6.34	2	381
DNMT3A	2	Missense	SNP	G	A	c.2644C>T	R882C	765	6.01	2	1162
DNMT3A	2	Missense	SNP	T	C	c.1933A>G	T645A	397	5.79	2	1685
DNMT3A	2	Frameshift	DEL	CTCATTCATGAAGACAGGAAAAT	C	c.2562_2583delATTTTCCTGTCTTCATGAATGA	E855fs*	893	5.71	2	1153
DNMT3A	2	Missense	SNP	C	A	c.1481G>T	C494F	323	5.26	2	1685
DNMT3A	2	Missense	SNP	A	G	c.2578T>C	p.W860R	253	5.14	3	164
DNMT3A	2	Missense	SNP	C	T	c.2387G>A	G796D	389	4.88	2	1463
DNMT3A	2	Missense	SNP	C	T	c.2246G>A	R749H	1563	4.67	2	901
DNMT3A	2	Missense	SNP	A	T	c.2042T>A	I681N	324	4.63	2	62
DNMT3A	2	Missense	SNP	G	A	c.1096C>T	R366C	1151	4.6	2	1167
DNMT3A	2	Missense	SNP	C	T	c.2645G>A	R882H	647	4.48	2	1347
DNMT3A	2	Missense	SNP	T	C	c.1933T>C	T645A	832	3.97	2	750
DNMT3A	2	Missense	SNP	G	T	c.2395C>A	P799T	536	3.73	2	1338
DNMT3A	2	Missense	SNP	A	C	c.1640T>G	p.L547R	731	3.69	3	1750
DNMT3A	2	Frameshift	DEL	CT	C	c.1718delA	p.Q573Rfs*78	2602	3.54	3	932
DNMT3A	2	Missense	SNP	G	A	c.2185C>T	R729W	685	3.5	2	1079
DNMT3A	2	Frameshift	DEL	CGATG	C	c.2146_2149delCATC	I715fs*	876	3.08	2	1158
DNMT3A	2	Missense	SNP	C	A	c.2186G>T	R729L	643	2.95	2	1065
DNMT3A	2	Missense	SNP	A	G	c.2264T>C	F755S	1523	2.82	2	1419
DNMT3A	2	Missense	SNP	A	G	c.2339T>C	I780T	1118	2.77	2	1613
DNMT3A	2	Frameshift	DEL	CT	C	c.2596delA	R866fs*	829	2.53	2	62

DNMT3A	2	Missense	SNP	A	G	c.2114T>C	I705T	806	2.48	2	1731
DNMT3A	2	Missense	SNP	G	C	c.2141C>G	S714C	953	2.41	2	927
DNMT3A	2	Splice site	SNP	C	T	c.1279+1G>A	null	519	1.54	3	164
DNMT3A	2	Splice site	SNP	C	T	c.1554+1G>A	null	301	1.33	3	1775
EP300	22	Missense	SNP	G	A	c.4199G>A	S1400N	133	31.58	2	1153
EP300	22	Deletion	DEL	GTGAGAAGTGTTTCAA	G	c.3603_3617delTGAGAAGTGTTTCAA	E1202_N1206del	639	14.71	2	94
EP300	22	Deletion	DEL	AGAT	A	c.4330_4332delGAT	D1444del	222	10.36	2	1685
ETV6	12	Missense	SNP	G	A	c.1058G>A	R353Q	935	51.98	2	1713
ETV6	12	Deletion	DEL	CAAACTAAACATT	C	c.1207_1218delAAACTAAACATT	403_406delKLNI	591	24.03	2	389
ETV6	12	Missense	SNP	T	G	c.1138T>G	p.W380G	316	7.59	3	1787
ETV6	12	Frameshift	DEL	CTA	C	c.417_418delTA	S139fs*	1555	7.07	2	338
ETV6	12	Missense	SNP	A	G	c.1177A>G	K393E	539	7.05	2	761
EZH2	7	Nonsense	SNP	C	T	c.1512G>A	W504*	376	12.77	2	532
FLT3	13	Missense	SNP	C	A	c.2503G>T	D835Y	839	33.73	2	110
GNAS	20	Missense	SNP	G	A	c.2531G>A	R844H	1550	6	2	282
GNB1	1	Missense	SNP	T	C	c.169A>G	K57E	1161	16.71	2	1014
GNB1	1	Missense	SNP	T	C	c.169A>G	K57E	1131	4.51	2	1139
GNB1	1	Missense	SNP	C	A	c.171G>T	K57N	1177	2.63	2	1014
GNB1	1	Missense	SNP	T	C	c.169A>G	K57E	1353	2.51	2	1602
GNB1	1	Missense	SNP	T	C	c.169T>C	K57E	2094	1.81	2	869
IDH1	2	Missense	SNP	G	C	c.394C>G	R132G	1016	44.78	2	136
IDH2	15	Missense	SNP	G	A	c.418C>T	R140W	1647	51.24	2	1661
IKZF1	7	Nonsense	SNP	C	T	c.1531C>T	R511*	530	15.47	2	110
IKZF3	17	Missense	SNP	A	C	c.485T>G	L162R	741	13.63	2	1297
JAK2	9	Missense	SNP	G	T	c.1849G>T	V617F	358	53.35	2	165
JAK2	9	Missense	SNP	G	T	c.1849G>T	V617F	536	17.54	2	382
JAK2	9	Missense	SNP	G	T	c.1849G>T	V617F	400	8.25	2	1623
JAK2	9	Missense	SNP	G	T	c.1849G>T	V617F	501	8.18	2	1563
JAK2	9	Missense	SNP	G	T	c.1849G>T	V617F	644	3.11	2	733
KRAS	12	Missense	SNP	G	T	c.64C>A	Q22K	349	3.72	2	427
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	155	86.45	2	699
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	240	55	2	389
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	226	46.02	2	1041
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	198	45.45	2	531
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	180	45	2	317
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	326	42.64	2	444
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	207	41.55	2	1093
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	244	39.34	2	1375
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	238	39.08	2	911
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	195	38.97	2	1350
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	172	37.79	2	1451
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	267	37.45	2	1018
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	202	36.14	2	621
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	218	35.78	2	476
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	202	35.64	2	1285
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	225	35.11	2	1016
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	239	33.89	2	1593
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	120	33.33	2	1171

MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	544	33.09	2	272
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	234	32.48	2	1059
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	82	31.71	2	1701
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	143	30.77	2	1153
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	138	28.99	2	123
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	119	28.57	2	1045
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	177	28.25	2	32
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	200	27.5	2	1134
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	528	27.46	2	491
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	175	27.43	2	1714
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	1045	26.99	3	459
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	446	26.91	2	493
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	272	26.47	2	999
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	144	25.69	2	1173
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	195	25.64	2	1127
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	145	25.52	2	94
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	193	25.39	2	551
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	189	24.87	2	1428
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	234	24.36	2	1359
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	182	24.18	2	604
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	149	24.16	2	1727
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	232	22.41	2	1306
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	766	22.19	2	278
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	167	21.56	2	247
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	262	21.37	2	1297
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	356	21.35	2	198
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	186	20.97	2	1130
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	263	20.91	2	1104
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	226	20.35	2	1553
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	323	20.12	2	152
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	258	19.77	2	430
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	275	19.64	2	1709
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	989	18.4	3	1737
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	228	17.98	2	1405
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	221	17.19	2	1472
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	144	16.67	2	1364
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	108	16.67	2	452
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	288	16.67	2	1452
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	703	16.22	3	1766
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	239	15.9	2	1388
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	211	15.64	2	1710

MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	232	15.52	2	1085
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	137	15.33	2	1713
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	164	15.24	2	1024
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	1363	15.11	3	1702
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	985	14.92	3	1769
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	229	14.85	2	592
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	162	14.81	2	1043
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	164	14.63	2	825
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	223	14.35	2	1068
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	231	14.29	2	1007
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	229	13.97	2	1042
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	254	13.78	2	1491
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	291	13.4	2	978
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	324	13.27	2	224
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	288	13.19	2	522
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	184	13.04	2	1168
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	210	12.86	2	353
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	281	12.81	2	1647
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	188	12.77	2	1542
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	192	12.5	2	1382
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	239	12.13	2	1478
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	727	12.1	3	1768
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	233	12.02	2	599
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	176	11.93	2	994
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	218	11.93	2	277
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	194	11.86	2	1429
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	137	11.68	2	979
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	1314	11.64	3	1751
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	417	11.51	2	43
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	210	11.43	2	1420
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	251	11.16	2	1556
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	242	11.16	2	1602
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	181	11.05	2	1020
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	156	10.9	2	959
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	232	10.78	2	517
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	233	10.73	2	735
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	255	10.59	2	1117
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	172	10.47	2	998
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	193	10.36	2	845
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	196	10.2	2	471
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	255	10.2	2	1613

MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	178	10.11	2	187
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	172	9.88	2	1521
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	204	9.8	2	1110
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	236	9.75	2	1571
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	267	9.74	2	1256
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	175	9.71	2	139
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	239	9.62	2	1319
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	148	9.46	2	1323
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	233	9.44	2	411
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	203	9.36	2	1733
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	142	9.15	2	1159
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	199	9.05	2	985
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	210	9.05	2	145
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	215	8.84	2	1296
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	215	8.84	2	1379
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	249	8.84	2	506
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	216	8.8	2	948
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	218	8.72	2	201
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	161	8.7	2	1167
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	242	8.68	2	1570
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	304	8.55	2	1706
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	211	8.53	2	1090
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	165	8.48	2	620
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	201	8.46	2	1234
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	142	8.45	2	719
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	242	8.26	2	1717
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	134	8.21	2	527
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	260	8.08	2	358
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	252	7.94	2	441
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	164	7.93	2	774
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	190	7.89	2	1628
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	206	7.77	2	1477
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	233	7.73	2	1502
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	261	7.66	2	377
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	185	7.57	2	489
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	265	7.55	2	468
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	187	7.49	2	1161
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	205	7.32	2	1495
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	263	7.22	2	1361
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	156	7.05	2	1366
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	227	7.05	2	113

MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	186	6.99	2	1061
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	290	6.9	2	563
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	175	6.86	2	1557
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	163	6.75	2	399
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	283	6.71	2	641
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	346	6.65	2	289
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	212	6.6	2	243
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	214	6.54	2	1679
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	276	6.52	2	1712
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	415	6.51	2	869
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	156	6.41	2	1277
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	250	6.4	2	1333
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	219	6.39	2	1338
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	440	6.36	2	282
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	192	6.25	2	569
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	197	6.09	2	445
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	183	6.01	2	1307
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	303	5.94	2	1761
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	186	5.91	2	541
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	203	5.91	2	1728
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	241	5.81	2	1309
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	729	5.76	3	1771
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	261	5.75	2	1120
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	316	5.7	2	705
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	217	5.53	2	761
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	256	5.47	2	1341
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	274	5.47	2	1681
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	187	5.35	2	143
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	206	5.34	2	1126
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	225	5.33	2	1137
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	210	5.24	2	168
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	210	5.24	2	431
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	383	5.23	2	931
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	250	5.2	2	1565
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	214	5.14	2	394
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	235	5.11	2	909
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	197	5.08	2	1179
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	261	4.98	2	907
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	322	4.97	2	658
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	289	4.84	2	975
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	269	4.83	2	1008

MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	414	4.83	3	1787
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	235	4.68	2	933
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	340	4.52	2	1525
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	155	4.516	2	1162
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	184	4.348	2	357
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	231	4.33	2	1106
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	278	4.32	2	608
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	302	4.3	2	903
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	967	4.24	3	158
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	332	4.217	2	385
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	288	4.17	2	1462
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	168	4.167	2	555
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	169	4.142	2	1036
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	291	4.12	2	897
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	195	4.103	2	1086
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	246	4.07	2	857
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	1089	4.04	3	341
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	200	4	2	1009
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	275	4	2	1538
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	299	4	2	1547
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	201	3.98	2	62
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	251	3.98	2	378
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	480	3.96	2	800
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	600	3.83	3	1755
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	183	3.825	2	1005
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	185	3.784	2	1148
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	1084	3.78	3	696
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	381	3.67	2	488
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	164	3.659	2	1138
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	550	3.64	2	381
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	275	3.64	2	874
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	278	3.6	2	1091
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	281	3.56	2	1347
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	229	3.493	2	130
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	180	3.333	2	324
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	332	3.31	2	715
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	708	3.25	3	1588
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	228	3.07	2	704
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	232	3.017	2	662
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	235	2.979	2	1295
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	270	2.963	2	128

MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	476	2.94	2	655
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	173	2.89	2	996
MYD88	3	Missense	SNP	T	C	c.854T>C	L265P	438	2.87	2	1636
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	387	2.84	2	1653
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	143	2.797	2	769
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	179	2.793	2	416
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	257	2.724	2	1119
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	258	2.713	2	754
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	370	2.703	2	649
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	389	2.7	2	1691
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	335	2.687	2	433
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	227	2.643	2	1308
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	346	2.6	2	125
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	390	2.564	2	100
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	157	2.548	2	867
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	317	2.524	2	750
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	590	2.48	2	961
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	202	2.475	2	1236
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	572	2.43	2	1574
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	420	2.381	2	659
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	173	2.312	2	419
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	828	2.29	3	252
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	220	2.273	2	293
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	222	2.252	2	475
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	222	2.252	2	448
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	185	2.162	2	953
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	464	2.155	2	1260
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	392	2.041	2	822
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	198	2.02	2	1244
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	200	2	2	1322
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	357	2	2	878
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	162	1.852	2	51
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	217	1.843	2	570
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	222	1.802	2	947
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	222	1.802	2	622
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	167	1.796	2	986
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	230	1.739	2	991
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	298	1.678	2	549
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	363	1.653	2	685
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	305	1.639	2	167
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	496	1.61	2	1683

MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	373	1.609	2	692
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	1012	1.58	3	1740
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	191	1.571	2	545
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	196	1.531	2	615
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	203	1.478	2	401
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	205	1.463	2	779
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	624	1.4	2	507
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	793	1.387	2	461
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	217	1.382	2	82
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	221	1.357	2	628
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	302	1.325	2	532
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	462	1.299	2	733
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	235	1.28	2	1736
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	239	1.255	2	1135
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	239	1.255	2	1063
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	251	1.195	2	593
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	348	1.149	2	390
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	964	1.14	3	466
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	442	1.131	2	346
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	180	1.111	2	456
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	288	1.042	2	336
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	392	1.02	2	1228
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	300	1	2	1259
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	428	0.935	2	849
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	808	0.87	3	164
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	1145	0.87	3	932
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	817	0.86	3	1775
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	970	0.82	3	1498
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	646	0.77	3	928
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	182	0.549	2	120
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	375	0.533	2	866
MYD88	3	Missense	SNP	T	C	c.794T>C	L265P	222	0.45	2	227
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	803	0.37	3	703
MYD88	3	Missense	SNP	T	C	c.794T>C	p.L265P	1441	0.07	3	1648
NF1	17	Splice site	SNP	T	A	c.2850+2T>A	null	579	2.42	3	1762
NOTCH1	9	Missense	SNP	T	C	c.4451A>G	p.N1484S	1287	19.58	3	1702
NOTCH1	9	Frameshift	DEL	CAG	C	c.7543_7544delCT	P2514fs*	989	2.63	2	1079
NOTCH2	1	Frameshift	DEL	TG	T	c.6910delG	P2303fs*	1445	2.08	2	641
NRAS	1	Missense	SNP	C	T	c.35G>A	G12D	1104	5.07	2	126
PPM1D	17	Nonsense	SNP	C	T	c.1654C>T	p.R552*	1762	6.7	3	928
PPM1D	17	Frameshift	DEL	ATTCTGGCCCCC	A	c.1626_1636delTTCTGGCCCCC	p.S543Dfs*5	1708	3.22	3	928
PPM1D	17	Frameshift	INS	C	CA	c.1547_1548insA	p.T517Nfs*11	1276	2.19	3	158

RAD21	8	Deletion	DEL	TTTG	T	c.1385_1387delCAA	T461del	173	44.51	2	830
RUNX1	21	Frameshift	INS	C	CG	c.1037_1037insC	R346fs*	298	45.97	2	136
RUNX1	21	Frameshift	INS	G	GACCA	c.390_390insTGGT	V131fs*	952	20.48	2	511
RUNX1	21	Frameshift	INS	C	CAT	c.1254_1254insAT	M419fs*	226	17.7	2	338
RUNX1	21	Frameshift	INS	C	CAG	c.296_296insCT	C99fs*	266	13.53	2	377
RUNX1	21	Frameshift	INS	C	CT	c.427_427insA	A142fs*	494	7.89	2	123
SF3B1	2	Missense	SNP	C	G	c.1998G>C	K666N	307	33.88	2	1529
SF3B1	2	Missense	SNP	T	C	c.2098A>G	K700E	355	27.04	2	143
SF3B1	2	Missense	SNP	C	A	c.1998G>T	K666N	498	25.7	2	1650
SF3B1	2	Missense	SNP	T	C	c.2098A>G	K700E	385	7.01	2	380
SF3B1	2	Missense	SNP	T	C	c.2098A>G	K700E	1081	4.35	2	69
SF3B1	2	Missense	SNP	T	C	c.2098A>G	K700E	390	4.1	2	1286
SF3B1	2	Missense	SNP	T	C	c.2098A>G	K700E	372	4.03	2	1331
SH2B3	12	Missense	SNP	G	A	c.1198G>A	E400K	97	53.61	2	614
SH2B3	12	Missense	SNP	T	C	c.1201T>C	Y401H	144	49.31	2	1701
SH2B3	12	Missense	SNP	G	A	c.1183G>A	E395K	353	48.73	2	1235
SH2B3	12	Missense	SNP	G	A	c.1198G>A	E400K	136	47.79	2	1491
SH2B3	12	Missense	SNP	G	A	c.1114G>A	p.V372M	1508	44.3	3	1610
SH2B3	12	Missense	SNP	C	T	c.1187C>T	T396M	153	42.48	2	570
SH2B3	12	Missense	SNP	C	T	c.724C>T	P242S	34	38.24	2	1012
SH2B3	12	Frameshift	INS	G	GCT	c.1037_1038insCT	G346fs*	2212	6.87	2	888
SH2B3	12	Missense	SNP	T	G	c.1291T>G	p.F431V	1243	3.38	3	1771
SMC1A	X	Deletion	DEL	CCTT	C	c.805_807delAAG	268delK	88	17.05	2	911
SRSF2	17	Missense	SNP	G	C	c.284C>G	P95R	145	56.55	2	1661
SRSF2	17	Missense	SNP	G	T	c.284C>A	P95H	136	51.47	2	136
SRSF2	17	Missense	SNP	G	A	c.284C>T	P95L	109	32.11	2	1014
SRSF2	17	Missense	SNP	G	A	c.284C>T	P95L	101	31.68	2	511
SRSF2	17	Missense	SNP	G	A	c.284C>T	P95L	54	27.78	2	1529
SRSF2	17	Missense	SNP	G	T	c.284C>A	P95H	116	21.55	2	324
SRSF2	17	Missense	SNP	G	T	c.284C>A	P95H	156	16.67	2	126
SRSF2	17	Missense	SNP	G	C	c.284C>G	p.P95R	1472	5.64	3	304
STAG2	X	Frameshift	INS	A	AT	c.59_60insT	H20fs*	646	95.2	2	1661
STAG2	X	Frameshift	DEL	CG	C	c.3398delG	R1133fs*	316	7.91	2	40
STAG2	X	Nonsense	SNP	G	T	c.3283G>T	E1095*	592	6.93	2	1161
TET2	4	Frameshift	INS	C	CT	c.3809_3810insT	T1270fs*	533	71.86	2	774
TET2	4	Missense	SNP	G	A	c.3515G>A	G1172D	1555	52.15	2	1579
TET2	4	Missense	SNP	A	G	c.3443A>G	Y1148C	2967	50.83	2	165
TET2	4	Missense	SNP	C	G	c.3609C>G	S1203R	292	48.29	2	1502
TET2	4	Deletion	DEL	AGAGCAT	A	c.5715_5720delGAGCAT	1906_1907delSM	78	47.44	2	43
TET2	4	Frameshift	INS	C	CG	c.3458_3459insG	A1153fs*	2159	47.01	2	1014
TET2	4	Frameshift	INS	G	GT	c.5633_5634insT	R1878fs*	85	45.88	2	1014
TET2	4	Missense	SNP	G	A	c.3637G>A	V1213M	273	43.59	2	856
TET2	4	Missense	SNP	C	G	c.5821C>G	P1941A	979	43.41	2	620
TET2	4	Frameshift	DEL	TC	T	c.822delC	I274fs*	1256	41.64	2	126
TET2	4	Frameshift	DEL	TTCATGGAGCATGTA	C	c.3867_3881delinsC	S1292fs*	750	38.53	2	1235
TET2	4	Frameshift	DEL	TTC	T	c.4251_4252delTC	V1417fs*	302	38.41	2	1416
TET2	4	Frameshift	DEL	GC	G	c.2965delC	K988fs*	856	37.73	2	126
TET2	4	Missense	SNP	T	G	c.3491T>G	p.M1164R	379	36.68	3	1780

TET2	4	Missense	SNP	G	A	c.3893G>A	C1298Y	1388	36.53	2	1416
TET2	4	Missense	SNP	C	T	c.5627C>T	A1876V	109	19.27	2	760
TET2	4	Frameshift	INS	G	GT	c.874_875insT	V292fs*	2228	15.84	2	1434
TET2	4	Frameshift	INS	T	TG	c.5539_5540insG	W1847fs*	500	15.8	2	1034
TET2	4	Frameshift	INS	A	AAAG	c.3997_3998insAAG	1333_1333M>KV	1392	10.27	2	996
TET2	4	Frameshift	INS	T	TG	c.2917_2918insG	C973fs*	669	8.97	2	1381
TET2	4	Nonsense	SNP	C	T	c.1576C>T	Q526*	1937	8.83	2	599
TET2	4	Nonsense	SNP	C	T	c.4333C>T	Q1445*	383	8.36	2	1650
TET2	4	Missense	SNP	A	G	c.4151A>G	D1384G	858	8.04	2	69
TET2	4	Frameshift	INS	G	GTCC	c.4097_4098insTCC	P1366dup	428	7.94	2	262
TET2	4	Frameshift	DEL	AT	A	c.3309delT	N1103fs*	492	5.49	2	168
TET2	4	Nonsense	SNP	C	T	c.2368C>T	Q790*	1233	5.35	2	1156
TET2	4	Missense	DNP	CC	AG	c.3776_3777CC>AG	T1259K	248	4.44	2	1155
TET2	4	Frameshift	DEL	GA	G	c.2098delA	L699fs*	716	4.05	2	961
TET2	4	Frameshift	DEL	CT	C	c.1389delT	p.N464Ifs*22	406	3.69	3	928
TET2	4	Frameshift	DEL	GCAGAGCTTTCTGGATC	G	c.5554_5569delCAGAGCTTTCTGGATC	E1851fs*	1140	3.68	2	73
TET2	4	Frameshift	INS	G	GA	c.4311_4312insA	E1437fs*	409	3.67	2	774
TET2	4	Frameshift	INS	T	TGC	c.2733_2734insGC	A911fs*	1568	2.49	2	1338
TET2	4	Frameshift	DEL	CCCACTCATGAGATGGATGG	C	c.5174_5192delCCACTCATGAGATGGATGG	P1725fs*	1136	2.2	2	1429
TET2	4	Frameshift	DEL	TG	T	c.1837delG	P612fs*	2654	1.73	2	641
TET2	4	Nonsense	SNP	C	T	c.3157C>T	p.Q1053*	2416	1.49	3	1702
TET2	4	Missense	SNP	A	G	c.5650A>G	p.T1884A	775	1.42	3	1738
TP53	17	Missense	SNP	T	C	c.704A>G	N235S	598	55.69	2	1319
TP53	17	Missense	SNP	A	T	c.558T>A	D186E	688	49.85	2	743
TP53	17	Missense	SNP	G	A	c.722C>T	S241F	476	46.64	2	1016
TP53	17	Missense	SNP	T	C	c.704A>G	N235S	563	44.4	2	1090
TP53	17	Missense	SNP	C	G	c.289G>C	V97L	182	41.21	2	277
TP53	17	Nonsense	SNP	G	A	c.916C>T	R306*	379	39.84	2	123
TP53	17	Frameshift	INS	G	GCCC	c.847_847insGGG	282_283insG	690	32.32	2	1043
TP53	17	Missense	SNP	T	C	c.578A>G	H193R	730	30.27	2	1381
TP53	17	Deletion	DEL	GCAAGTCACAGACTT	G	c.358_371delAAGTCTGTGACTTGinsC	K120fs*	201	25.87	2	1725
TP53	17	Nonsense	SNP	G	A	c.574C>T	Q192*	878	15.03	2	123
TP53	17	Nonsense	SNP	G	A	c.586C>T	R196*	840	14.52	2	527
TP53	17	Missense	SNP	G	A	c.844C>T	R282W	365	12.05	2	1542
TP53	17	Missense	SNP	A	G	c.584T>C	I195T	878	11.05	2	1306
TP53	17	Missense	SNP	T	C	c.701A>G	Y234C	666	10.51	2	414
TP53	17	Missense	SNP	G	A	c.844C>T	R282W	357	9.24	2	1478
TP53	17	Missense	SNP	T	C	c.488A>G	Y163C	118	8.47	2	517
TP53	17	Missense	SNP	T	C	c.701A>G	Y234C	791	8.47	2	1070
TP53	17	Missense	SNP	T	C	c.716A>G	N239S	408	6.62	2	399
TP53	17	Frameshift	DEL	CA	C	c.256delT	P85fs*	213	5.63	2	760
TP53	17	Missense	SNP	G	T	c.843C>A	D281E	431	5.1	2	845
TP53	17	Missense	SNP	G	C	c.833C>G	P278R	509	4.91	2	1042
TP53	17	Missense	SNP	T	C	c.578A>G	H193R	625	4.8	2	1557
TP53	17	Missense	SNP	T	C	c.745A>G	R249G	568	3.17	2	1359
TP53	17	Missense	SNP	A	C	c.809T>G	F270C	400	3	2	1350
TP53	17	Missense	SNP	C	T	c.743G>A	R248Q	558	2.87	2	927
TP53	17	Missense	SNP	G	A	c.817C>T	R273C	500	2.8	2	1197
TP53	17	Frameshift	INS	C	CG	c.455dupC	p.P153Afs*28	941	2.02	3	928
TP53	17	Missense	SNP	C	T	c.646G>A	p.V216M	739	1.49	3	928
TP53	17	Missense	SNP	C	T	c.743G>A	p.R248Q	573	1.05	3	1588
U2AF1	21	Missense	SNP	G	A	c.101C>T	S34F	435	39.31	2	338
U2AF1	21	Missense	SNP	G	A	c.101C>T	p.S34F	430	25.81	3	1787
U2AF1	21	Missense	SNP	T	G	c.470A>C	Q157P	988	4.05	2	1650
U2AF1	21	Missense	SNP	T	C	c.470T>C	Q157R	1144	3.85	2	1229
ZRSR2	X	Frameshift	DEL	GCA	G	c.1252_1253delCA	R417fs*	124	11.29	2	1435

Table S3. Patient characteristics of symptomatic Waldenström Macroglobulinemia cohort.

	Total	CH		*p-value*
		Yes	No	
	n = 440 (%)	n = 61 (14)	n = 379 (86)	
Age at diagnosis				
Median (range)	61 (22 - 90)	64 (39 - 84)	61 (22 - 90)	*0.04*†
Age groups				
20-29	1 (0)	0 (0)	1 (0)	*0.03*^
30-39	10 (2)	2 (3)	8 (2)	
40-49	55 (12)	3 (5)	52 (14)	
50-59	126 (29)	14 (23)	112 (30)	
60-69	166 (38)	26 (43)	140 (37)	
70-79	82 (19)	16 (26)	66 (17)	
Age at NGS				
Median (range)	68 (33 - 93)	72 (44 - 85)	67 (33 - 93)	*<0.001*†
Sex				
Female	161 (37)	25 (41)	136 (36)	*0.48*‡
Male	279 (63)	36 (59)	243 (64)	
Ashkenazi				
Yes	26 (6)	3 (5)	23 (6)	*>0.99*‡
No	414 (94)	58 (95)	356 (94)	
Amyloidosis				
Yes	19 (4)	7 (11)	12 (3)	*0.009*‡
No	421 (96)	54 (89)	367 (97)	
DVT, PE, Stroke, or Clot vs none				
Yes	42 (10)	12 (20)	30 (8)	*0.008*‡
None	398 (90)	49 (80)	349 (92)	
CAD, MI				
Yes	43 (10)	6 (10)	37 (10)	*>0.99*‡
No	397 (90)	55 (90)	342 (90)	
Smoking				
Yes	171 (39)	28 (46)	143 (38)	*0.26*‡
No	261 (59)	32 (52)	229 (60)	
Missing	*8 (2)*	*1 (2)*	*7 (2)*	
Alcohol				
Yes	295 (67)	41 (67)	254 (67)	*>0.99*‡
No	119 (27)	17 (28)	102 (27)	
Missing	*26 (6)*	*3 (5)*	*23 (6)*	

EMD at diagnosis				
Yes	56 (13)	7 (11)	49 (13)	*0.84*‡
No	383 (87)	54 (89)	329 (87)	
Missing	*1 (0)*	*0 (0)*	*1 (0)*	
EMD at any point				
Yes	105 (24)	19 (31)	86 (23)	*0.19*‡
No	334 (76)	42 (69)	292 (77)	
Missing	*1 (0)*	*0 (0)*	*1 (0)*	
Other cancers				
Yes	77 (18)	13 (21)	64 (17)	*0.47*‡
No	363 (82)	48 (79)	315 (83)	
No. of therapies, any				
Median (range)	2 (0 - 10)	2 (0 - 10)	1 (0 - 9)	*0.09*†
No. of therapies, pre-NGS				
Median (range)	1 (0 - 10)	1 (0 - 10)	1 (0 - 7)	*0.08*†
Ibrutinib pre-NGS				
Yes	86 (20)	14 (23)	72 (19)	*0.49*‡
No	354 (80)	47 (77)	307 (81)	
Cytotoxic therapies, any				
Yes	194 (44)	32 (52)	162 (43)	*0.17*‡
No	246 (56)	29 (48)	217 (57)	
No. of therapies				
0	246 (56)	29 (48)	217 (57)	*0.06*^
1	137 (31)	21 (34)	116 (31)	
2	40 (9)	6 (10)	34 (9)	
3	12 (3)	4 (7)	8 (2)	
4	3 (1)	0 (0)	3 (1)	
5	2 (0)	1 (2)	1 (0)	
Cytotoxic therapies, pre-NGS				
Yes	141 (32)	26 (43)	115 (30)	*0.08*‡
No	299 (68)	35 (57)	264 (70)	
No. of therapies				
0	299 (68)	35 (57)	264 (70)	*0.14*^
1	98 (22)	18 (30)	80 (21)	
2	31 (7)	6 (10)	25 (7)	
3	9 (2)	2 (3)	7 (2)	
4	2 (0)	0 (0)	2 (1)	
5	1 (0)	0 (0)	1 (0)	
Prior chemotherapy				

Yes	9 (2)	1 (2)	8 (2)	*>0.99*‡
No	431 (98)	60 (98)	371 (98)	
BM involvement at diagnosis (%)				
Median (range)	55 (4 - 95)	40 (5 - 90)	60 (4 - 95)	*0.32*†
Missing	*81 (18)*	*14 (23)*	*67 (18)*	
BM involvement at NGS (%)				
Median (range)	50 (0 - 95)	50 (1 - 95)	50 (0 - 95)	*0.47*†
Missing	*10 (2)*	*3 (5)*	*7 (2)*	
BM involvement at progression (%)				
Median (range)	70 (5 - 100)	70 (10 - 100)	60 (5 - 95)	*0.33*†
Missing	*303 (69)*	*40 (66)*	*263 (69)*	
BM involvement in aspirate (%)				
Median (range)	3 (1 - 27)	3 (1 - 23)	3 (1 - 27)	*0.66*†
Missing	*235 (53)*	*28 (46)*	*207 (55)*	
		Kappa		
Kappa (Yes, No)				
No	93 (21)	13 (21)	80 (21)	*>0.99*‡
Yes	347 (79)	48 (79)	299 (79)	
Kappa level at diagnosis				
Median (range)	39.50 (5.80 - 5000.00)	23.10 (20.70 - 46.00)	40.75 (5.80 - 5000.00)	*0.88*†
Missing	*421 (96)*	*58 (95)*	*363 (96)*	
Kappa level at NGS				
Median (range)	40.10 (5.10 - 1805.00)	37.60 (9.90 - 140.90)	40.10 (5.10 - 1805.00)	*0.95*†
Missing	*339 (77)*	*47 (77)*	*292 (77)*	
Kappa level at Tx Baseline				
Median (range)	43.30 (1.11 - 4110.00)	25.30 (1.20 - 742.10)	46.75 (1.11 - 4110.00)	*0.16*†
Missing	*305 (69)*	*40 (66)*	*265 (70)*	
Kappa level at Tx Latest				
Median (range)	25.80 (1.60 - 6790.00)	20.20 (1.60 - 215.60)	27.40 (3.14 - 6790.00)	*0.44*†
Missing	*333 (76)*	*45 (74)*	*288 (76)*	
		Lambda		
Lambda (Yes, No)				
No	334 (76)	46 (75)	288 (76)	*>0.99*‡
Yes	106 (24)	15 (25)	91 (24)	
Lambda level at diagnosis				
Median (range)	10.50 (1.20 - 70.20)	10.30 (9.40 - 11.30)	10.70 (1.20 - 70.20)	*0.91*†
Missing	*422 (96)*	*58 (95)*	*364 (96)*	
Lambda level at NGS				
Median (range)	10.10 (0.53 - 610.20)	12.35 (5.60 - 132.30)	9.90 (0.53 - 610.20)	*0.18*†
Missing	*339 (77)*	*47 (77)*	*292 (77)*	

Lambda level at Tx Baseline				
Median (range)	10.90 (0.59 - 2817.40)	11.30 (1.20 - 228.70)	10.90 (0.59 - 2817.40)	*0.52*†
Missing	*304 (69)*	*40 (66)*	*264 (70)*	
Lambda level at Tx Latest				
Median (range)	8.800 (0.560 - 1319.600)	7.800 (0.573 - 131.200)	9.300 (0.560 - 1319.600)	*0.74*†
Missing	*333 (76)*	*45 (74)*	*288 (76)*	
		IgG		
IgG at Dx				
Median (range)	710 (203 - 1620)	646 (216 - 1070)	739 (203 - 1620)	*0.32*†
Missing	*400 (91)*	*54 (89)*	*346 (91)*	
IgG at NGS				
Median (range)	509 (49 - 5093)	582 (179 - 1360)	490 (49 - 5093)	*0.92*†
Missing	*323 (73)*	*45 (74)*	*278 (73)*	
IgG at Tx Baseline				
Median (range)	466 (51 - 4934)	376 (57 - 1592)	480 (51 - 4934)	*0.04*†
Missing	*128 (29)*	*17 (28)*	*111 (29)*	
IgG at Tx Latest				
Median (range)	440 (55 - 2928)	372 (55 - 1263)	442 (56 - 2928)	*0.18*†
Missing	*89 (20)*	*11 (18)*	*78 (21)*	
		IgA		
IgA at Dx				
Median (range)	63 (7 - 245)	65 (15 - 187)	62 (7 - 245)	*0.57*†
Missing	*400 (91)*	*54 (89)*	*346 (91)*	
IgA at NGS				
Median (range)	51 (5 - 382)	37 (5 - 238)	54 (5 - 382)	*0.89*†
Missing	*323 (73)*	*45 (74)*	*278 (73)*	
IgA at Tx Baseline				
Median (range)	32.5 (5.0 - 576.0)	29.5 (5.0 - 261.0)	33.0 (5.0 - 576.0)	*0.53*†
Missing	*128 (29)*	*17 (28)*	*111 (29)*	
IgA at Tx Latest				
Median (range)	42 (5 - 496)	34 (5 - 231)	44 (5 - 496)	*0.25*†
Missing	*90 (20)*	*11 (18)*	*79 (21)*	
		IgM		
IgM at Dx				
Median (range)	2447 (437 - 9078)	2304 (474 - 6400)	2910 (437 - 9078)	*0.44*†
Missing	*394 (90)*	*52 (85)*	*342 (90)*	
IgM at NGS				
Median (range)	1706 (15 - 8310)	2131 (57 - 7700)	1690 (15 - 8310)	*> 0.99*†
Missing	*321 (73)*	*44 (72)*	*277 (73)*	

IgM at Tx Baseline				
Median (range)	2799 (25 - 10300)	2334 (100 - 8480)	2962 (25 - 10300)	*0.28*[†]
Missing	*101 (23)*	*16 (26)*	*85 (22)*	
IgM at Tx Latest				
Median (range)	854 (15 - 8236)	816 (23 - 5932)	858 (15 - 8236)	*0.70*[†]
Missing	*72 (16)*	*10 (16)*	*62 (16)*	

[†]Wilcoxon rank-sum test, ^Cochran-Armitage test, [‡]Fisher's exact test

Table S4. Hematologic and immunologic parameters of symptomatic Waldenström Macroglobulinemia patients at time of NGS assay.

	Total	CH		*p-value*
		Yes	No	
	n = 440 (%)	n = 61 (14)	n = 379 (86)	
Absolute bands				
Median (range)	0.07 (0.00 - 0.98)	0.08 (0.03 - 0.33)	0.07 (0.00 - 0.98)	*0.96*†
Missing	*414 (94)*	*53 (87)*	*361 (95)*	
Absolute basos				
Median (range)	0.04 (0.00 - 0.66)	0.04 (0.00 - 0.66)	0.04 (0.00 - 0.19)	*0.83*†
Missing	*86 (20)*	*12 (20)*	*74 (20)*	
Absolute blasts				
Median (range)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	-
Missing	*375 (85)*	*46 (75)*	*329 (87)*	
Absolute EOS				
Median (range)	0.09 (0.00 - 1.33)	0.08 (0.00 - 1.31)	0.09 (0.00 - 1.33)	*> 0.99*†
Missing	*83 (19)*	*14 (23)*	*69 (18)*	
Absolute lymphs				
Median (range)	1.27 (0.02 - 85.00)	1.02 (0.14 - 4.39)	1.32 (0.02 - 85.00)	*0.03*†
Missing	*87 (20)*	*15 (25)*	*72 (19)*	
Absolute metas				
Median (range)	0.15 (0.02 - 1.31)	0.08 (0.02 - 1.31)	0.16 (0.05 - 0.71)	*0.58*†
Missing	*428 (97)*	*58 (95)*	*370 (98)*	
Absolute monos				
Median (range)	0.62 (0.03 - 3.91)	0.62 (0.22 - 1.73)	0.62 (0.03 - 3.91)	*0.97*†
Missing	*87 (20)*	*16 (26)*	*71 (19)*	
Absolute myelos				
Median (range)	0.05 (0.04 - 0.12)	-	0.05 (0.04 - 0.12)	-
Missing	*437 (99)*	*61 (100)*	*376 (99)*	
Absolute neuts				
Median (range)	3.59 (0.50 - 31.60)	3.64 (1.06 - 14.99)	3.57 (0.50 - 31.60)	*> 0.99*†
Missing	*85 (19)*	*15 (25)*	*70 (18)*	
Absolute NRBC				
Median (range)	0 (0 - 0)	-	0 (0 - 0)	-
Missing	*437 (99)*	*61 (100)*	*376 (99)*	

Absolute plasma cells				
Median (range)	1.24 (0.04 - 14.22)	-	1.24 (0.04 - 14.22)	-
Missing	*436 (99)*	*61 (100)*	*375 (99)*	
Absolute reactive lymphs				
Median (range)	0.03 (0.01 - 0.04)	-	0.03 (0.01 - 0.04)	-
Missing	*438 (100)*	*61 (100)*	*377 (99)*	
Bands				
Median (range)	1.0 (0.0 - 9.0)	1.5 (1.0 - 5.0)	1.0 (0.0 - 9.0)	*0.26*†
Missing	*414 (94)*	*53 (87)*	*361 (95)*	
Basos				
Median (range)	0.7 (0.0 - 3.1)	0.8 (0.0 - 3.1)	0.7 (0.0 - 2.6)	*0.98*†
Missing	*90 (20)*	*17 (28)*	*73 (19)*	
Beta2				
Median (range)	3.3 (1.4 - 30.5)	4.0 (2.0 - 30.5)	3.2 (1.4 - 22.5)	*0.004*†
Missing	*191 (43)*	*29 (48)*	*162 (43)*	
Blasts				
Median (range)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	*> 0.99*†
Missing	*375 (85)*	*46 (75)*	*329 (87)*	
CRP				
Median (range)	4.3 (0.6 - 6.3)	-	4.3 (0.6 - 6.3)	-
Missing	*437 (99)*	*61 (100)*	*376 (99)*	
EOS				
Median (range)	1.6 (0.0 - 21.0)	1.6 (0.0 - 7.5)	1.6 (0.0 - 21.0)	*0.78*†
Missing	*93 (21)*	*19 (31)*	*74 (20)*	
HCT				
Median (range)	34.5 (19.1 - 49.3)	33.8 (24.6 - 45.6)	34.8 (19.1 - 49.3)	*0.73*†
Missing	*36 (8)*	*5 (8)*	*31 (8)*	
HGB				
Median (range)	11.6 (6.2 - 17.1)	11.2 (7.7 - 15.8)	11.6 (6.2 - 17.1)	*0.71*†
Missing	*37 (8)*	*5 (8)*	*32 (8)*	
LDH				
Median (range)	152 (73 - 408)	150 (73 - 324)	153 (74 - 408)	*0.72*†
Missing	*325 (74)*	*37 (61)*	*288 (76)*	
Lymphs				
Median (range)	22.8 (0.6 - 70.0)	22.7 (3.4 - 49.5)	22.8 (0.6 - 70.0)	*0.45*†

Missing	*90 (20)*	*17 (28)*	*73 (19)*	
MCH				
Median (range)	30.7 (18.7 - 44.7)	31.1 (18.7 - 38.9)	30.6 (19.2 - 44.7)	*0.57*†
Missing	*37 (8)*	*4 (7)*	*33 (9)*	
MCHC				
Median (range)	33.5 (29.2 - 47.7)	33.6 (30.2 - 36.0)	33.5 (29.2 - 47.7)	*0.80*†
Missing	*37 (8)*	*4 (7)*	*33 (9)*	
MCV				
Median (range)	91.1 (61.9 - 112.5)	91.6 (61.9 - 108.1)	91.0 (62.1 - 112.5)	*0.72*†
Missing	*37 (8)*	*4 (7)*	*33 (9)*	
Metas				
Median (range)	2 (1 - 4)	1 (1 - 4)	2 (1 - 3)	*0.70*†
Missing	*428 (97)*	*58 (95)*	*370 (98)*	
Monos				
Median (range)	10.3 (1.1 - 39.0)	11.6 (1.4 - 39.0)	10.0 (1.1 - 34.6)	*0.15*†
Missing	*88 (20)*	*16 (26)*	*72 (19)*	
MPV				
Median (range)	7.8 (5.8 - 13.1)	7.8 (6.1 - 10.5)	7.7 (5.8 - 13.1)	*0.64*†
Missing	*52 (12)*	*8 (13)*	*44 (12)*	
Myelos				
Median (range)	1 (1 - 1)	-	1 (1 - 1)	-
Missing	*437 (99)*	*61 (100)*	*376 (99)*	
Neuts				
Median (range)	63.0 (23.0 - 94.7)	64.2 (30.0 - 94.7)	62.9 (23.0 - 94.2)	*0.71*†
Missing	*71 (16)*	*11 (18)*	*60 (16)*	
NRBC				
Median (range)	0 (0 - 1)	0 (0 - 1)	0 (0 - 1)	*0.66*†
Missing	*94 (21)*	*15 (25)*	*79 (21)*	
Plasma cells				
Median (range)	10 (1 - 60)	-	10 (1 - 60)	-
Missing	*436 (99)*	*61 (100)*	*375 (99)*	
PLT				
Median (range)	218 (23 - 692)	226 (35 - 692)	216 (23 - 630)	*0.23*†
Missing	*75 (17)*	*14 (23)*	*61 (16)*	
RBC				

Median (range)	3.81 (1.87 - 7.23)	3.66 (2.62 - 7.23)	3.84 (1.87 - 5.52)	*0.38*†
Missing	*41 (9)*	*5 (8)*	*36 (9)*	
RDW				
Median (range)	14.3 (12.0 - 25.4)	15.1 (12.7 - 21.7)	14.2 (12.0 - 25.4)	*0.08*†
Missing	*36 (8)*	*4 (7)*	*32 (8)*	
Reactive lymphs				
Median (range)	1 (1 - 1)	-	1 (1 - 1)	-
Missing	*438 (100)*	*61 (100)*	*377 (99)*	
WBC				
Median (range)	5.99 (0.72 - 97.71)	5.85 (1.56 - 32.79)	6.00 (0.72 - 97.71)	*0.55*†
Missing	*41 (9)*	*6 (10)*	*35 (9)*	

†Wilcoxon rank-sum test

Table S5. Patient characteristics of 26 Waldenström Macroglobulinemia patients with *TP53* mutation.

		CH		
	Total	**Yes**	**No**	***p-value***
	n = 26 (%)	**n = 6 (23)**	**n = 20 (77)**	
Age at diagnosis				
Median (range)	63 (33 - 88)	64 (55 - 88)	63 (33 - 75)	0.63†
20-29	-	0 (0)	0 (0)	0.42^
30-39	2 (8)	0 (0)	2 (10)	
40-49	-	0 (0)	0 (0)	
50-59	8 (31)	2 (33)	6 (30)	
60-69	10 (38)	2 (33)	8 (40)	
70-79	6 (23)	2 (33)	4 (20)	
Age at NGS				
Median (range)	72 (37 - 88)	77 (75 - 88)	70 (37 - 79)	*0.002†*
Sex				
Female	10 (38)	2 (33)	8 (40)	> 0.99‡
Male	16 (62)	4 (67)	12 (60)	
Ashkenazi				
Yes	3 (12)	-	3 (15)	> 0.99‡
No	23 (88)	6 (100)	17 (85)	
Amyloidosis				
Yes	-	-	-	> 0.99‡
No	26 (100)	6 (100)	20 (100)	
DVT, PE, Stroke, Clot				
No	26 (100)	6 (100)	20 (100)	-
DVT, PE, Stroke, or Clot vs none				
Yes	-	-	-	> 0.99‡
No	26 (100)	6 (100)	20 (100)	
Smoking				
Yes	13 (50)	3 (50)	10 (50)	> 0.99‡
No	13 (50)	3 (50)	10 (50)	
Alcohol				
Yes	24 (92)	4 (67)	20 (100)	*0.046‡*
No	2 (8)	2 (33)	-	
EMD at diagnosis				
Yes	1 (4)	-	1 (5)	> 0.99‡
No	25 (96)	6 (100)	19 (95)	

EMD at any point				
Yes	8 (31)	2 (33)	6 (30)	> 0.99‡
No	18 (69)	4 (67)	14 (70)	
Other cancers				
Yes	6 (23)	1 (17)	5 (25)	> 0.99‡
No	20 (77)	5 (83)	15 (75)	
No. of therapies, any				
Median (range)	2 (0 - 10)	4 (1 - 10)	2 (0 - 7)	*0.035*‡
No. of therapies, pre-NGS				
Median (range)	1 (0 - 10)	4 (1 - 10)	1 (0 - 6)	*0.039*‡
Ibrutinib pre-NGS				
Yes	7 (27)	4 (67)	3 (15)	*0.028*‡
No	19 (73)	2 (33)	17 (85)	
Cytotoxic therapies, any				
Yes	10 (38)	5 (83)	5 (25)	*0.018*‡
No	16 (62)	1 (17)	15 (75)	
0	16 (62)	1 (17)	15 (75)	*0.010*^
1	5 (19)	2 (33)	3 (15)	
2	3 (12)	2 (33)	1 (5)	
3	1 (4)	0 (0)	1 (5)	
4	-	0 (0)	0 (0)	
5	1 (4)	1 (17)	0 (0)	
Cytotoxic therapies, pre-NGS				
Yes	9 (35)	5 (83)	4 (20)	*0.010*‡
No	17 (65)	1 (17)	16 (80)	
0	17 (65)	1 (17)	16 (80)	*0.008*^
1	4 (15)	2 (33)	2 (10)	
2	3 (12)	2 (33)	1 (5)	
3	1 (4)	0 (0)	1 (5)	
4	-	0 (0)	0 (0)	
5	1 (4)	1 (17)	0 (0)	
Prior chemotherapy				
Yes	1 (4)	-	1 (5)	> 0.99‡
No	25 (96)	6 (100)	19 (95)	
BM involvement at diagnosis (%)				
Median (range)	70 (20 - 95)	40 (20 - 90)	75 (20 - 95)	0.28†
Missing	*5 (19)*	*1 (17)*	*4 (20)*	
BM involvement at NGS (%)				

Median (range)	65 (5 - 95)	30 (5 - 80)	75 (10 - 95)	*0.032*†
BM involvement at progression (%)				
Median (range)	90 (50 - 95)	92 (90 - 95)	80 (50 - 95)	> 0.99‡
Missing	*17 (65)*	*4 (67)*	*13 (65)*	

†Wilcoxon rank-sum test, ^Cochran-Armitage test, ‡Fisher's exact test

Table S6. Patient characteristics of asymptomatic Waldenström Macroglobulinemia cohort.

		CH		
	Total	**Yes**	**No**	***p-value***
	n = 147 (%)	**n = 20 (14)**	**n = 127 (86)**	
Age at diagnosis				
Median (range)	63 (39 - 89)	66 (39 - 86)	63 (39 - 89)	*0.31*†
Age groups				
30-39	2 (1)	1 (5)	1 (1)	*0.37*^
40-49	18 (12)	1 (5)	17 (13)	
50-59	40 (27)	4 (20)	36 (28)	
60-69	48 (33)	7 (35)	41 (32)	
70-79	39 (27)	7 (35)	32 (25)	
Age at NGS				
Median (range)	66 (40 - 89)	66 (53 - 86)	65 (40 - 89)	*0.23*†
Sex				
Female	69 (47)	7 (35)	62 (49)	*0.34*‡
Male	78 (53)	13 (65)	65 (51)	
Diagnosis				
MGUS	31 (21)	4 (20)	27 (21)	*> 0.99*‡
Smoldering WM	116 (79)	16 (80)	100 (79)	
Ashkenazi				
Yes	30 (20)	4 (20)	26 (20)	*> 0.99*‡
No	117 (80)	16 (80)	101 (80)	
Amyloidosis				
Yes	3 (2)	1 (5)	2 (2)	*0.36*‡
No	143 (97)	19 (95)	124 (98)	
Missing	*1 (1)*	*0 (0)*	*1 (1)*	
DVT, PE, Stroke, or Clot vs none				
Yes	15 (10)	2 (10)	13 (10)	*> 0.99*‡
None	132 (90)	18 (90)	114 (90)	
CAD, MI				
Yes	14 (10)	2 (10)	12 (9)	*> 0.99*‡
No	133 (90)	18 (90)	115 (91)	
Smoking				
Yes	72 (49)	11 (55)	61 (48)	*0.63*‡
No	75 (51)	9 (45)	66 (52)	
Alcohol				
Yes	108 (73)	14 (70)	94 (74)	*0.78*‡

No	34 (23)	5 (25)	29 (23)	
Missing	*5 (3)*	*1 (5)*	*4 (3)*	
EMD at diagnosis				
Yes	12 (8)	2 (10)	10 (8)	*0.67*‡
No	135 (92)	18 (90)	117 (92)	
EMD at any point				
Yes	11 (7)	3 (15)	8 (6)	*0.17*‡
No	136 (93)	17 (85)	119 (94)	
Other cancers				
Yes	31 (21)	3 (15)	28 (22)	*0.57*‡
No	116 (79)	17 (85)	99 (78)	
No. of therapies, any				
Median (range)	0 (0 - 3)	0 (0 - 1)	0 (0 - 3)	*0.69*†
No. of therapies, pre-NGS				
Median (range)	0 (0 - 1)	0 (0 - 0)	0 (0 - 1)	*0.58*†
Ibrutinib pre-NGS				
Yes	0 (0)	0 (0)	0 (0)	*> 0.99*‡
No	147 (100)	20 (100)	127 (100)	
Cytotoxic therapies, any				
Yes	1 (1)	1 (5)	0 (0)	*0.14*‡
No	146 (99)	19 (95)	127 (100)	
Cytotoxic therapies, pre-NGS				
Yes	0 (0)	0 (0)	0 (0)	*> 0.99*‡
No	147 (100)	20 (100)	127 (100)	
Prior chemotherapy				
Yes	9 (6)	1 (5)	8 (6)	*> 0.99*‡
No	138 (94)	19 (95)	119 (94)	
BM involvement at diagnosis (%)				
Median (range)	20.0 (0.3 - 95.0)	20.0 (5.0 - 80.0)	20.0 (0.3 - 95.0)	*0.87*†
Missing	*22 (15)*	*3 (15)*	*19 (15)*	
BM involvement at NGS (%)				
Median (range)	20 (1 - 95)	40 (5 - 95)	20 (1 - 95)	*0.46*†
Missing	*7 (5)*	*1 (5)*	*6 (5)*	
BM involvement at progression (%)				
Median (range)	40 (10 - 95)	68 (40 - 95)	40 (10 - 80)	*0.28*†
Missing	*136 (93)*	*18 (90)*	*118 (93)*	
BM involvement in aspirate (%)				
Median (range)	3 (1 - 20)	4 (2 - 13)	3 (1 - 20)	*0.19*†
Missing	*70 (48)*	*10 (50)*	*60 (47)*	
		Kappa		

Kappa (Yes, No)				
No	33 (22)	7 (35)	26 (20)	*0.16*‡
Yes	114 (78)	13 (65)	101 (80)	
Kappa level at diagnosis				
Median (range)	22.15 (8.30 - 829.30)	18.04 (10.60 - 25.48)	22.15 (8.30 - 829.30)	*0.52*†
Missing	*105 (71)*	*18 (90)*	*87 (69)*	
Kappa level at NGS				
Median (range)	25.45 (3.38 - 2648.30)	30.85 (6.30 - 2648.30)	24.95 (3.38 - 407.10)	*0.31*†
Missing	*55 (37)*	*4 (20)*	*51 (40)*	
Kappa level at Tx Baseline				
Median (range)	17.10 (6.84 - 2300.00)	-	17.10 (6.84 - 2300.00)	-
Missing	*138 (94)*	*20 (100)*	*118 (93)*	
Kappa level at Tx Latest				
Median (range)	28.7 (6.6 - 2015.2)	84.7 (32.8 - 2015.2)	25.9 (6.6 - 95.2)	*0.02*†
Missing	*122 (83)*	*15 (75)*	*107 (84)*	
		Lambda		
Lambda (Yes, No)				
No	110 (75)	12 (60)	98 (77)	*0.16*‡
Yes	37 (25)	8 (40)	29 (23)	
Lambda level at diagnosis				
Median (range)	10.25 (2.60 - 105.90)	38.96 (25.63 - 52.30)	10.00 (2.60 - 105.90)	*0.09*†
Missing	*105 (71)*	*18 (90)*	*87 (69)*	
Lambda level at NGS				
Median (range)	12.05 (0.84 - 472.10)	13.35 (7.20 - 335.90)	11.45 (0.84 - 472.10)	*0.11*†
Missing	*55 (37)*	*4 (20)*	*51 (40)*	
Lambda level at Tx Baseline				
Median (range)	12.10 (7.15 - 778.00)	-	12.10 (7.15 - 778.00)	-
Missing	*138 (94)*	*20 (100)*	*118 (93)*	
Lambda level at Tx Latest				
Median (range)	11.0 (2.5 - 110.5)	12.0 (5.4 - 57.2)	10.8 (2.5 - 110.5)	*0.84*†
Missing	*122 (83)*	*15 (75)*	*107 (84)*	
		IgG		
IgG at Dx				
Median (range)	683 (235 - 1979)	831 (639 - 1155)	672 (235 - 1979)	*0.29*†
Missing	*96 (65)*	*17 (85)*	*79 (62)*	
IgG at NGS				
Median (range)	654 (120 - 2670)	674 (120 - 1328)	644 (184 - 2670)	*0.57*†
Missing	*41 (28)*	*1 (5)*	*40 (31)*	
IgG at Tx Baseline				
Median (range)	730 (407 - 1390)	-	730 (407 - 1390)	-

Missing	*137 (93)*	*20 (100)*	*117 (92)*	
IgG at Tx Latest				
Median (range)	662 (117 - 2510)	752 (117 - 1367)	612 (135 - 2510)	*0.20*†
Missing	*39 (27)*	*6 (30)*	*33 (26)*	
		IgA		
IgA at Dx				
Median (range)	75 (7 - 493)	134 (56 - 152)	75 (7 - 493)	*0.41*†
Missing	*96 (65)*	*17 (85)*	*79 (62)*	
IgA at NGS				
Median (range)	75 (5 - 1404)	76 (17 - 351)	74 (5 - 1404)	*0.59*†
Missing	*41 (28)*	*1 (5)*	*40 (31)*	
IgA at Tx Baseline				
Median (range)	98.7 (38.0 - 383.0)	-	98.7 (38.0 - 383.0)	-
Missing	*137 (93)*	*20 (100)*	*117 (92)*	
IgA at Tx Latest				
Median (range)	68 (5 - 3059)	96 (25 - 369)	66 (5 - 3059)	*0.10*†
Missing	*39 (27)*	*6 (30)*	*33 (26)*	
		IgM		
IgM at Dx				
Median (range)	1539 (174 - 4947)	716 (323 - 2390)	1552 (174 - 4947)	*0.53*†
Missing	*90 (61)*	*15 (75)*	*75 (59)*	
IgM at NGS				
Median (range)	1228 (134 - 7554)	1658 (312 - 4815)	1191 (134 - 7554)	*0.31*†
Missing	*41 (28)*	*1 (5)*	*40 (31)*	
IgM at Tx Baseline				
Median (range)	1645 (315 - 4680)	-	1645 (315 - 4680)	-
Missing	*137 (93)*	*20 (100)*	*117 (92)*	
IgM at Tx Latest				
Median (range)	1264 (84 - 6140)	1404 (279 - 6130)	1260 (84 - 6140)	*0.41*†
Missing	*37 (25)*	*5 (25)*	*32 (25)*	

†Wilcoxon rank-sum test, ^Cochran-Armitage test, ‡Fisher's exact test

Table S7. Patient characteristics of 15 Waldenström Macroglobulinemia patients with secondary MDS, AML or ALL.

		Somatic mutations	
	Total	**Yes**	**No**
	n = 15 (%)	**n = 14 (93)**	**n = 1 (7)**
Age at diagnosis			
Median (range)	70 (55 - 88)	70 (55 - 88)	78 (78 - 78)
Age groups			
50-59	2 (13)	2 (14)	0 (0)
60-69	5 (33)	5 (36)	0 (0)
70-79	8 (53)	7 (50)	1 (100)
Age at NGS			
Median (range)	77 (61 - 88)	77 (61 - 88)	78 (78 - 78)
Sex			
Female	2 (13)	1 (7)	1 (100)
Male	13 (87)	13 (93)	0 (0)
Diagnosis			
Smoldering WM	2 (13)	2 (14)	0 (0)
WM	13 (87)	12 (86)	1 (100)
Ashkenazi			
Yes	0 (0)	0 (0)	0 (0)
No	15 (100)	14 (100)	1 (100)
Amyloidosis			
Yes	0 (0)	0 (0)	0 (0)
No	15 (100)	14 (100)	1 (100)
DVT, PE, Stroke, or Clot vs none			
Yes	0 (0)	0 (0)	0 (0)
None	15 (100)	14 (100)	1 (100)
Smoking			
Yes	9 (60)	9 (64)	0 (0)
No	6 (40)	5 (36)	1 (100)
Alcohol			
Yes	11 (73)	10 (71)	1 (100)
No	3 (20)	3 (21)	0 (0)
Missing	*1 (7)*	*1 (7)*	*0 (0)*
EMD at diagnosis			
Yes	2 (13)	2 (14)	0 (0)
No	13 (87)	12 (86)	1 (100)
EMD at any point			
Yes	4 (27)	4 (29)	0 (0)
No	11 (73)	10 (71)	1 (100)
Other cancers			
Yes	3 (20)	3 (21)	0 (0)
No	12 (80)	11 (79)	1 (100)
No. of therapies, any			
Median (range)	1 (0 - 6)	1 (0 - 6)	1 (1 - 1)
No. of therapies, pre-NGS			

Median (range)	1 (0 - 6)	1 (0 - 6)	0 (0 - 0)
Ibrutinib pre-NGS			
Yes	1 (7)	1 (7)	0 (0)
No	14 (93)	13 (93)	1 (100)
Cytotoxic therapies, any			
Yes	6 (40)	5 (36)	1 (100)
No	9 (60)	9 (64)	0 (0)
No. of therapies			
0	9 (60)	9 (64)	0 (0)
1	4 (27)	3 (21)	1 (100)
2	1 (7)	1 (7)	0 (0)
5	1 (7)	1 (7)	0 (0)
Cytotoxic therapies, pre-NGS			
Yes	4 (27)	4 (29)	0 (0)
No	11 (73)	10 (71)	1 (100)
No. of therapies			
0	11 (73)	10 (71)	1 (100)
1	2 (13)	2 (14)	0 (0)
2	1 (7)	1 (7)	0 (0)
5	1 (7)	1 (7)	0 (0)
Prior chemotherapy			
Yes	0 (0)	0 (0)	0 (0)
No	15 (100)	14 (100)	1 (100)
BM involvement at diagnosis (%)			
Median (range)	50 (5 - 95)	50 (5 - 95)	60 (60 - 60)
Missing	*3 (20)*	*3 (21)*	*0 (0)*
BM involvement at time of NGS (%)			
Median (range)	10 (0 - 90)	10 (0 - 90)	0 (0)
Missing	*1 (7)*	*0 (0)*	*1 (100)*
BM involvement at progression (%)			
Median (range)	30 (15 - 90)	30 (15 - 90)	0 (0)
Missing	*12 (80)*	*11 (79)*	*1 (100)*
BM involvement in aspirate (%)			
Median (range)	2 (1 - 6)	2 (1 - 6)	1 (1 - 1)
Missing	*8 (53)*	*8 (57)*	*0 (0)*
	Kappa		
Kappa (Yes, No)			
No	1 (7)	1 (7)	0 (0)
Yes	14 (93)	13 (93)	1 (100)
Kappa level at diagnosis			
Median (range)	145.3 (45.7 - 245.0)	145.3 (45.7 - 245.0)	-
Missing	*13 (87)*	*12 (86)*	*1 (100)*
Kappa level at time of NGS			
Median (range)	36.0 (27.7 - 39.3)	36.0 (27.7 - 39.3)	-
Missing	*12 (80)*	*11 (79)*	*1 (100)*
Kappa level at Tx Baseline			
Median (range)	205.8 (21.3 - 390.3)	21.3 (21.3 - 21.3)	390.3 (390.3 - 390.3)
Missing	*13 (87)*	*13 (93)*	*0 (0)*

Kappa level at Tx Latest			
Median (range)	16.9 (16.7 - 17.1)	17.1 (17.1 - 17.1)	16.7 (16.7 - 16.7)
Missing	*13 (87)*	*13 (93)*	*0 (0)*
Lambda			
Lambda (Yes, No)			
No	12 (80)	11 (79)	1 (100)
Yes	3 (20)	3 (21)	0 (0)
Lambda level at diagnosis			
Median (range)	120.2 (14.5 - 225.9)	120.2 (14.5 - 225.9)	-
Missing	*13 (87)*	*12 (86)*	*1 (100)*
Lambda level at time of NGS			
Median (range)	11.8 (8.9 - 14.8)	11.8 (8.9 - 14.8)	-
Missing	*12 (80)*	*11 (79)*	*1 (100)*
Lambda level at Tx Baseline			
Median (range)	12 (9 - 14)	14 (14 - 14)	9 (9 - 9)
Missing	*13 (87)*	*13 (93)*	*0 (0)*
Lambda level at Tx Latest			
Median (range)	7.5 (4.2 - 10.8)	10.8 (10.8 - 10.8)	4.2 (4.2 - 4.2)
Missing	*13 (87)*	*13 (93)*	*0 (0)*
IgG			
IgG at Dx			
Median (range)	949 (720 - 1753)	949 (720 - 1753)	-
Missing	*12 (80)*	*11 (79)*	*1 (100)*
IgG at time of NGS			
Median (range)	701 (456 - 1040)	701 (456 - 1040)	-
Missing	*12 (80)*	*11 (79)*	*1 (100)*
IgG at Tx Baseline			
Median (range)	417 (183 - 846)	416 (183 - 846)	533 (533 - 533)
Missing	*8 (53)*	*8 (57)*	*0 (0)*
IgG at Tx Latest			
Median (range)	516 (111 - 1429)	552 (111 - 1429)	314 (314 - 314)
Missing	*5 (33)*	*5 (36)*	*0 (0)*
IgA			
IgA at Dx			
Median (range)	134 (118 - 202)	134 (118 - 202)	-
Missing	*12 (80)*	*11 (79)*	*1 (100)*
IgA at time of NGS			
Median (range)	77 (73 - 104)	77 (73 - 104)	-
Missing	*12 (80)*	*11 (79)*	*1 (100)*
IgA at Tx Baseline			
Median (range)	33 (10 - 96)	32 (10 - 96)	55 (55 - 55)
Missing	*8 (53)*	*8 (57)*	*0 (0)*
IgA at Tx Latest			
Median (range)	45 (5 - 130)	50 (5 - 130)	40 (40 - 40)
Missing	*5 (33)*	*5 (36)*	*0 (0)*
IgM			
IgM at Dx			
Median (range)	1280 (1153 - 6230)	1280 (1153 - 6230)	-

Missing	*12 (80)*	*11 (79)*	*1 (100)*
IgM at time of NGS			
Median (range)	587 (446 - 1260)	587 (446 - 1260)	-
Missing	*12 (80)*	*11 (79)*	*1 (100)*
IgM at Tx Baseline			
Median (range)	2060 (50 - 6430)	2345 (86 - 6430)	50 (50 - 50)
Missing	*6 (40)*	*6 (43)*	*0 (0)*
IgM at Tx Latest			
Median (range)	450 (17 - 3638)	576 (37 - 3638)	17 (17 - 17)
Missing	*5 (33)*	*5 (36)*	*0 (0)*

Table S8. Treatments received at any point and pre-NGS. Treatments given for all patients, for asymptomatic WM patients and symptomatic WM patients.

	All patients N = 587 (%)		Asymptomatic WM N = 147 (%)		Symptomatic WM N = 440 (%)	
Therapy	**Any**	**Pre-NGS**	**Any**	**Pre-NGS**	**Any**	**Pre-NGS**
None	168 (29)	291 (50)	142 (97)	145 (99)	26 (6)	146 (33)
Other	224 (38)	278 (47)	4 (3)	5 (3)	220 (50)	273 (62)
Bendamustine	130 (22)	72 (12)	1 (1)	-	129 (29)	72 (16)
Fludarabine	24 (4)	22 (4)	-	-	24 (5)	22 (5)
CD-R	17 (3)	16 (3)	-	-	17 (4)	16 (4)
CHOP	17 (3)	12 (2)	-	-	17 (4)	12 (3)
CDR	16 (3)	15 (3)	-	-	16 (4)	15 (3)
R-CHOP	14 (2)	10 (2)	-	-	14 (3)	10 (2)
Cyclophosphamide	12 (2)	12 (2)	-	-	12 (3)	12 (3)
Chlorambucil	11 (2)	11 (2)	-	-	11 (2)	11 (2)
R-CP	8 (1)	8 (1)	-	-	8 (2)	8 (2)
Cytoxan	8 (1)	6 (1)	-	-	8 (2)	6 (1)
CyBorD	7 (1)	7 (1)	-	-	7 (2)	7 (2)
R-CVP	7 (1)	7 (1)	-	-	7 (2)	7 (2)
Cladribine	6 (1)	6 (1)	-	-	6 (1)	6 (1)
RCP	6 (1)	6 (1)	-	-	6 (1)	6 (1)
RCHOP	5 (1)	2 (0)	-	-	5 (1)	2 (0)
R-CD	3 (1)	3 (1)	-	-	3 (1)	3 (1)
CP-R	3 (1)	3 (1)	-	-	3 (1)	3 (1)
RICE	3 (1)	1 (0)	-	-	3 (1)	1 (0)
RCD	2 (0)	2 (0)	-	-	2 (0)	2 (0)
CPR	2 (0)	2 (0)	-	-	2 (0)	2 (0)
DCR	2 (0)	2 (0)	-	-	2 (0)	2 (0)
Busulfan	1 (0)	1 (0)	-	-	1 (0)	1 (0)
CRD	1 (0)	1 (0)	-	-	1 (0)	1 (0)
BEAM	1 (0)	1 (0)	-	-	1 (0)	1 (0)
FCR	1 (0)	1 (0)	-	-	1 (0)	1 (0)
RCOP	1 (0)	1 (0)	-	-	1 (0)	1 (0)
hyperCVAD	1 (0)	1 (0)	-	-	1 (0)	1 (0)
EPOCH	1 (0)	1 (0)	-	-	1 (0)	1 (0)
VR-CAP	1 (0)	-	-	-	1 (0)	-
RCAP	1 (0)	1 (0)	-	-	1 (0)	1 (0)

ESHAP	1 (0)	1 (0)	-	-	1 (0)	1 (0)
Gemcitabine	1 (0)	-	-	-	1 (0)	-
Oxaliplatin	1 (0)	-	-	-	1 (0)	-

SUPPLEMENTARY FIGURES

Figure S1. Study workflow.

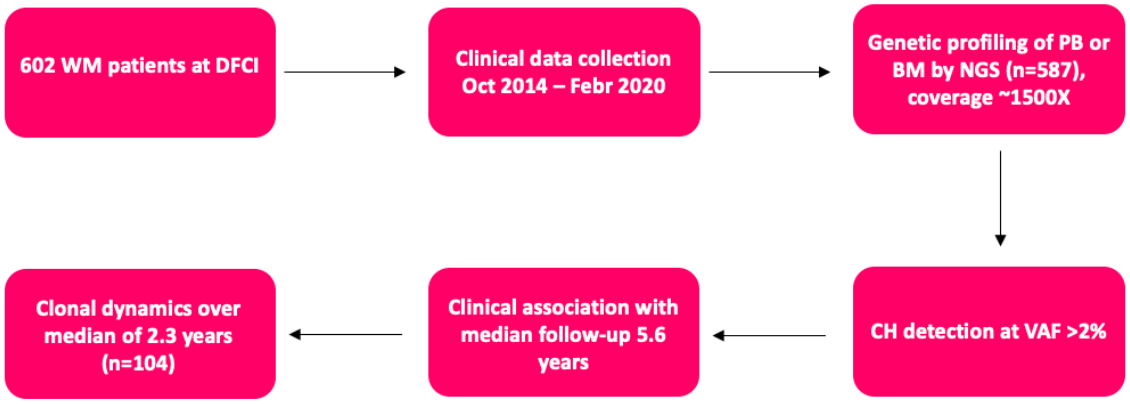
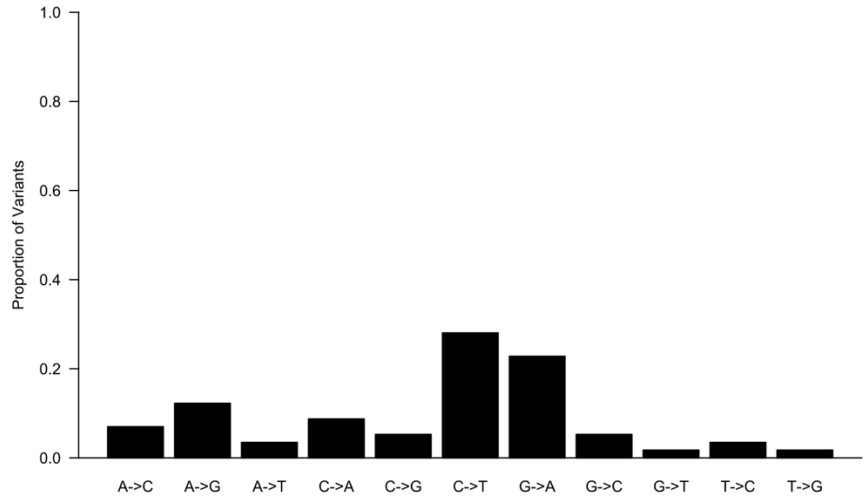


Figure S2 Mutational properties for all 602 Waldenström Macroglobulinemia patients. (A) Distribution of the types of single-nucleotide base-pair changes seen in all detected mutations. (B) Distribution of VAF among different variants.

A



B

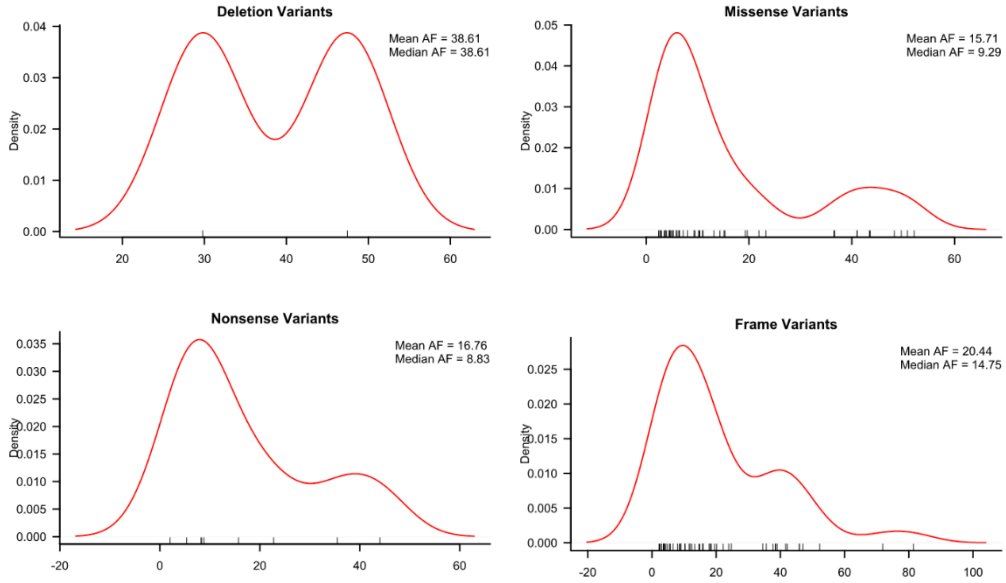


Figure S3. Mutational spectrum of all detected somatic mutations in patients with Waldenström Macroglobulinemia. A) Number of patients harboring mutations in 1, 2, 3, 4 and 5 different genes. (B) The total number of patients harboring one or more mutations in each gene. (C) The maximum VAF attained by each of the 258 patients with a somatic mutation. (D) The maximum VAF attained by each of the 81 patients with CH.

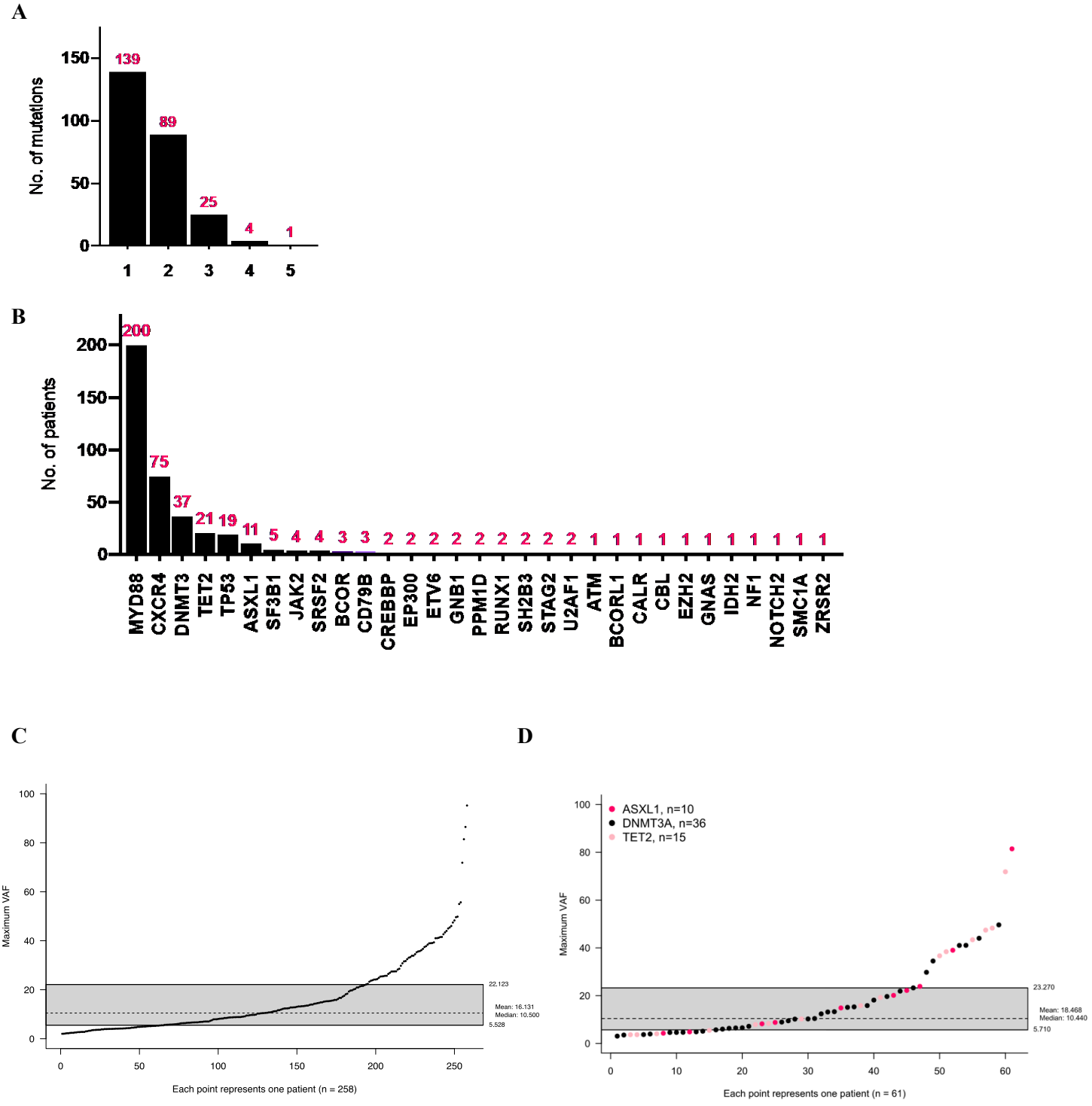
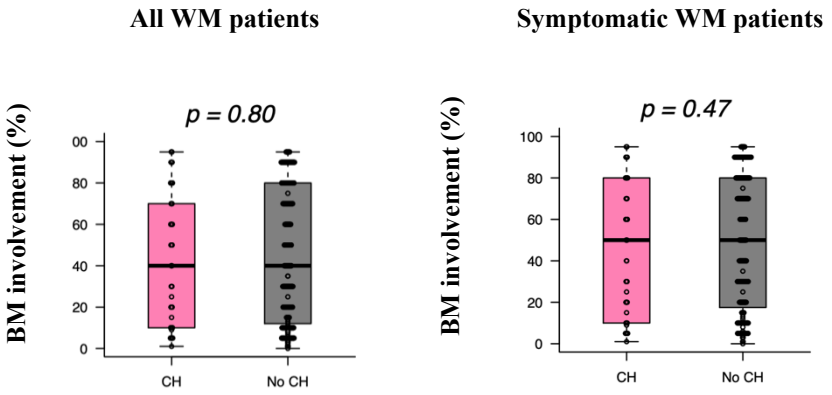
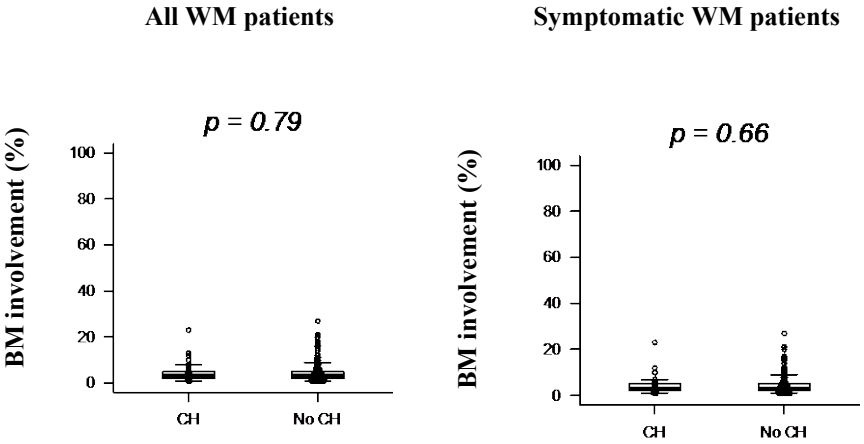


Figure S4. Correlation BM infiltration and *MYD88* status with CH-DTA detection in Waldenstrom Macroglobulinemia patients. (A) Barplot comparing detected plasma cell percentage in BM biopsies of patients with and without a CH-DTA mutation detected. Shown for the complete cohort of WM patients (left) and for the symptomatic WM patients only (right). (B) Barplot comparing detected plasma cell percentage in BM aspirates of patients with and without a CH-DTA mutation detected. Shown for the complete cohort of WM patients (left) and for the symptomatic WM patients only (right). (C) Frequency of CH-DTA mutations according to *MYD88* mutational status as detected with PCR.

A



B



C

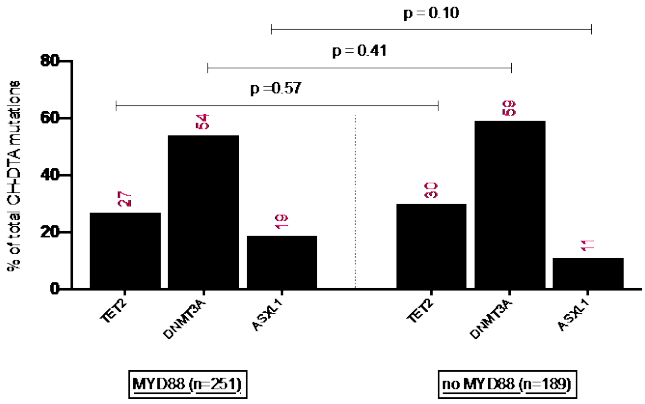
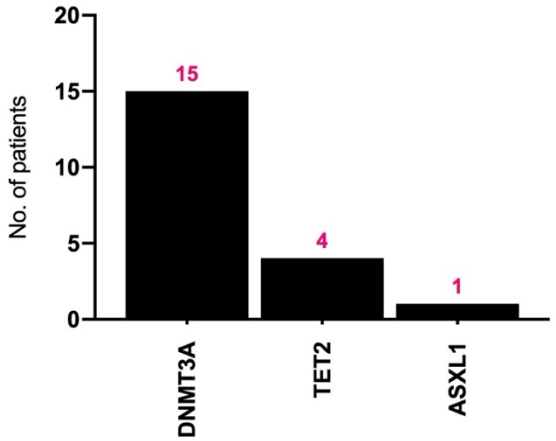
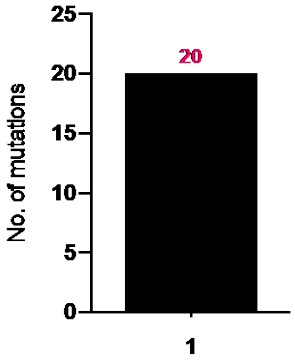


Figure S5. Mutational spectrum in patients with IgM MGUS and smoldering Waldenström Macroglobulinemia. (A) The total number of IgM MGUS and SWM patients harboring one or more mutations in each gene. (B) Number of IgM MGUS and SWM patients harboring mutations in 1 gene. (C) Mutation frequency of MYD88 and CXCR4 mutations per disease stage. (D) The maximum VAF attained by each of the 81 patients with a somatic mutation. (E) The maximum VAF attained by each of the 20 patients with CH.

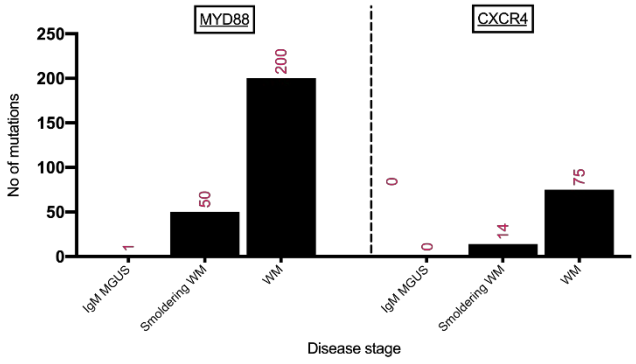
A



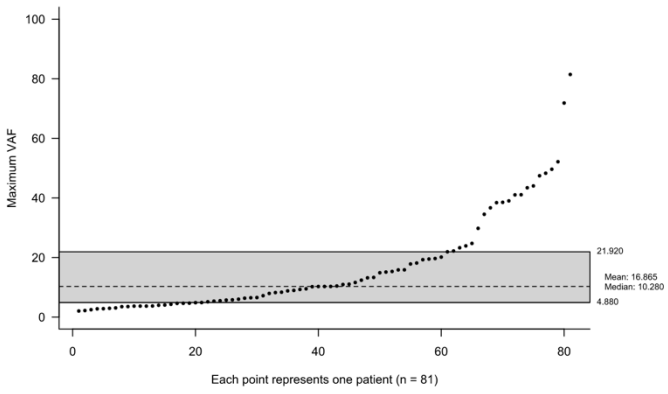
B



C



D



E

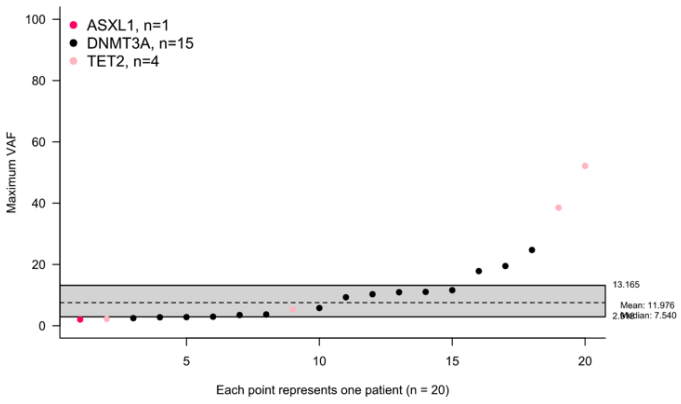
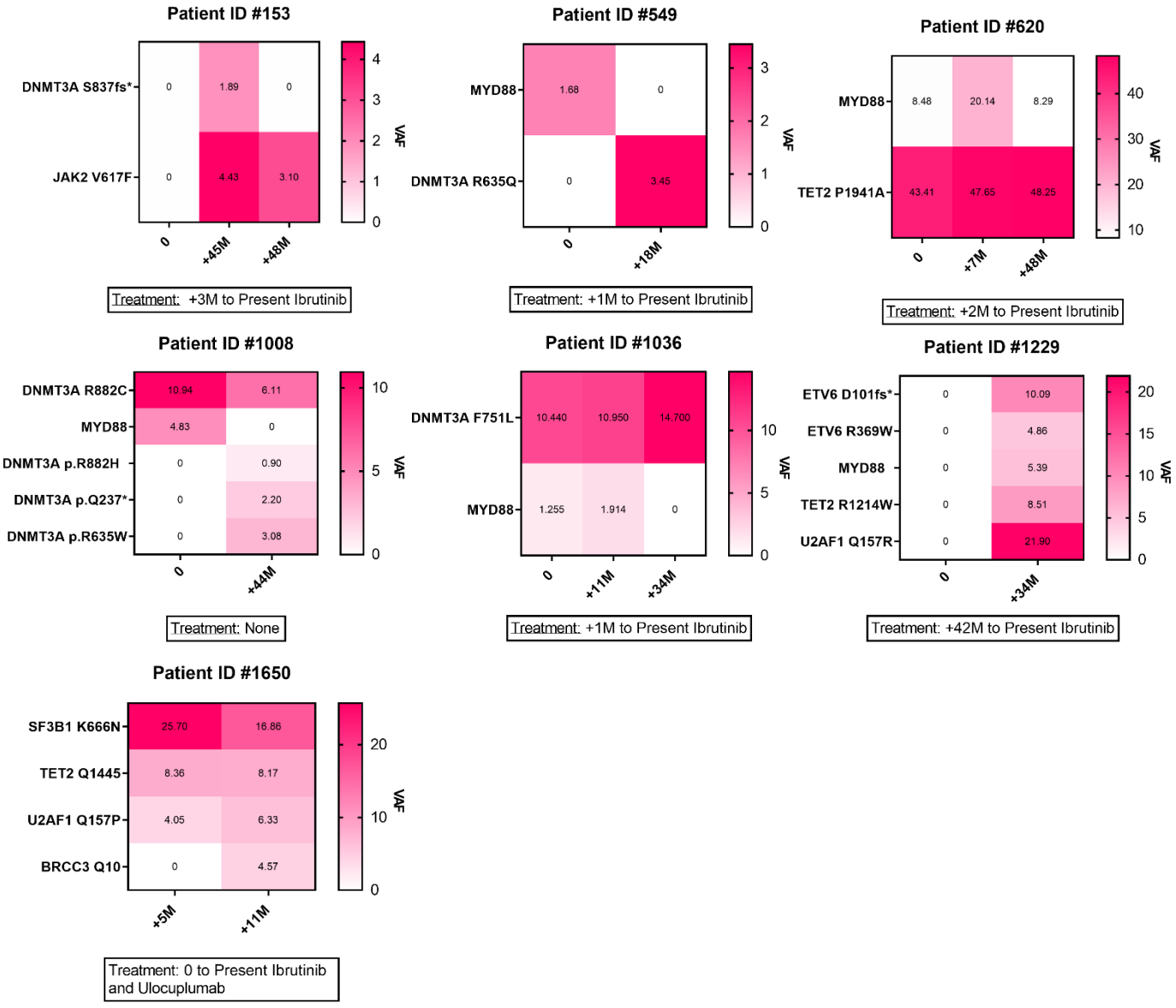


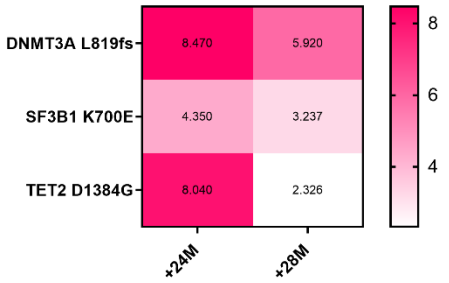
Figure S6 CH dynamics. Heatmaps for the clonal dynamics of 23 WM patients with >1 NGS test and any detected mutation (mutations with VAF <2% are also depicted). Each row in the heatmap is a single mutation; each column is one NSG assay timepoint. The right legend denotes the VAF detected, with darker shades of pink indicating higher VAF. Values within each square depict VAF detected. The legend below the heatmaps indicate the timepoint relative to the NSG date in months and the given therapy at that timepoint. (A) Heatmaps for patients that did not receive therapy or received chemotherapy-free regiments. (B) Heatmaps for patients that received at least one chemotherapy-consisting regimen.

A.



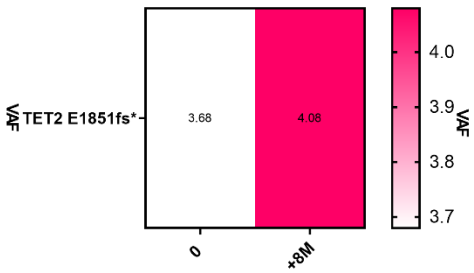
B.

Patient ID #69



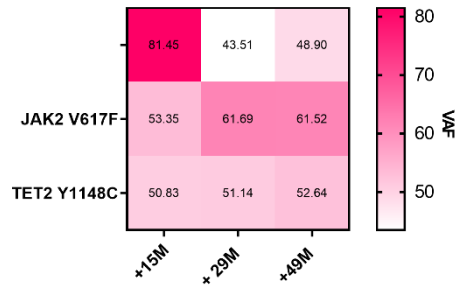
Treatment: 0 to +19M Carfilxomib, Dexamethasone and Rituximab.

Patient ID #73



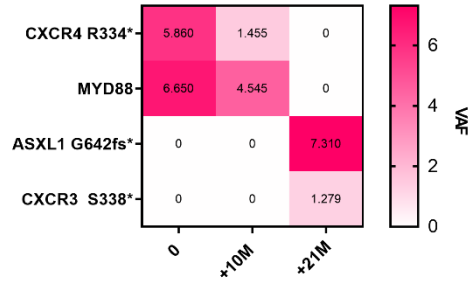
Treatment: +1M to +8 M Ixazomib, Dexamethason and Rituximab. + 8M to +18 M Bendamustine and Rituximab

Patient ID #165



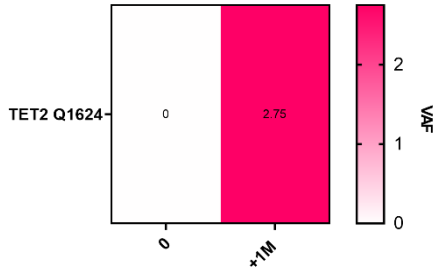
Treatment: 0 to +6M RCP, +9M to +15M Ibrutinib, +15 M to Present Ruxolitinib

Patient ID #289



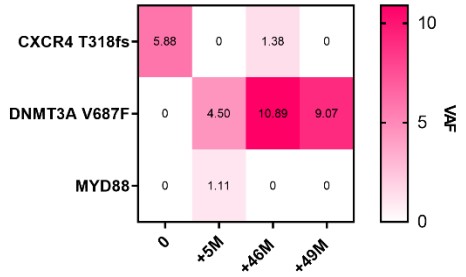
Treatment: 0 to +17M Ixazomib, Dexamethason and Rituximab.

Patient ID #535



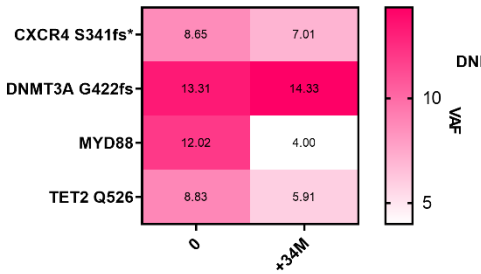
Treatment: +1 to +4M Rituximab and Bendamustine, +12M Rituximab, +24M to +27M Cytoxan, Bortezomib, Dexamethason

Patient ID #582



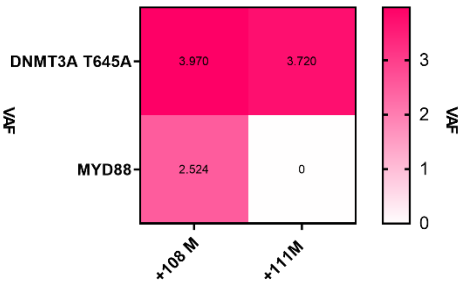
Treatment: 0 to +25M R-CHOP and Rituximab maintenance, +47M to Present RICE.

Patient ID #599



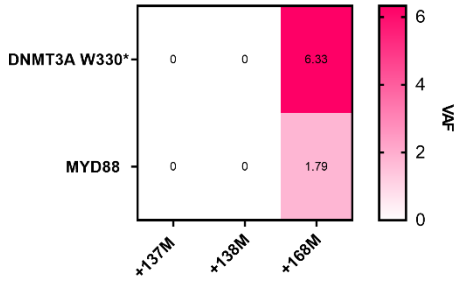
Treatment: +35M to +40M Bendamustine

Patient ID #750



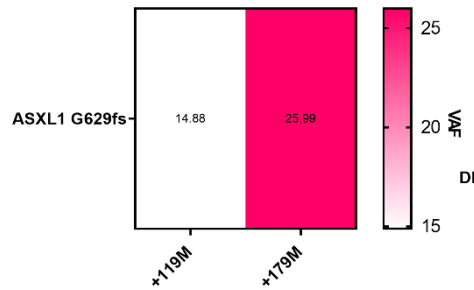
Treatment: 0 Rituximab, +12M Fludarabine, + 14M RCAP, +96M to Present Ibrutinib

Patient ID #804



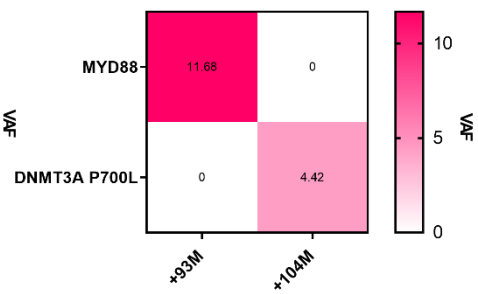
Treatment: 0 to +24M R-CHOP and Rituximab maintenance, +36M to +39 M Velcade and Rituximab, +54M to +58M Enzastaurin, +58M to +84M Cytoxan and Velcade, +115M to +118M Oprozomib, +118 M to +137M Ibrutinib, +138M to +158M Bendamustine and Ofatumumab.

Patient ID #930



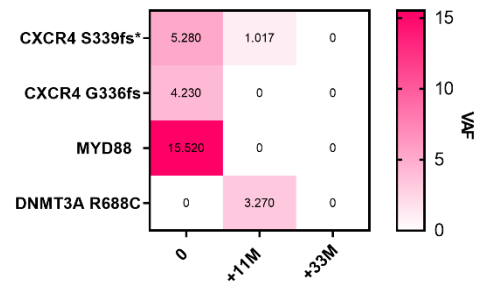
Treatment: 0 Rituximab, +12M Fludarabine, +24M Bortezomib and Rituximab, +36M CyBorD, +84M Everolimus, +96M Bendamustine, +107M Rituximab, +124 M to 180M Ibrutinib, 180M to Present Dasatanib.

Patient ID #979



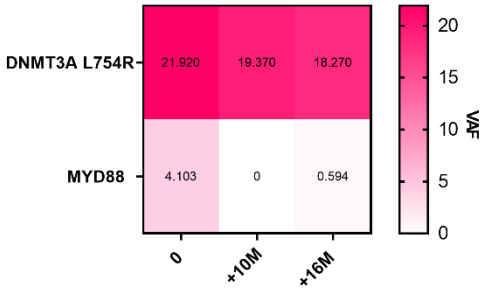
Treatment: 0 Bortezomib and Rituximab, +12M Enzaustarin, +24M Parabinostat, +76M to+94M Ibrutinib, +94M to +118M Venetoclax

Patient ID #1085



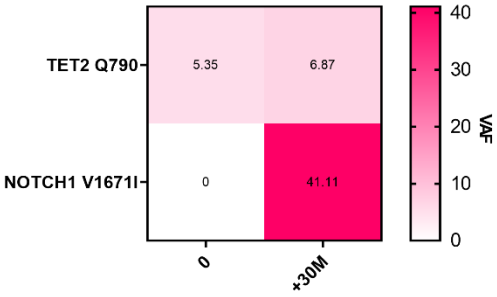
Treatment: +1M to +5M Bendamustine, +6M to Present Venetoclax

Patient ID #1086



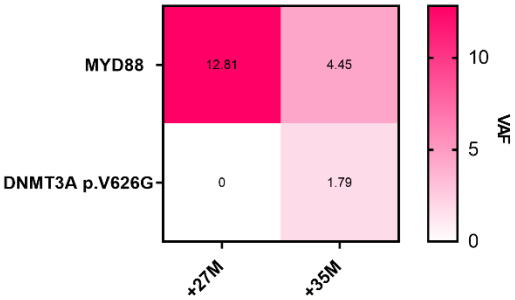
Treatment: 0 to +3M 2017 CDR, +3M to +6M Ibrutinib, +7M to Present Venetoclax

Patient ID #1156



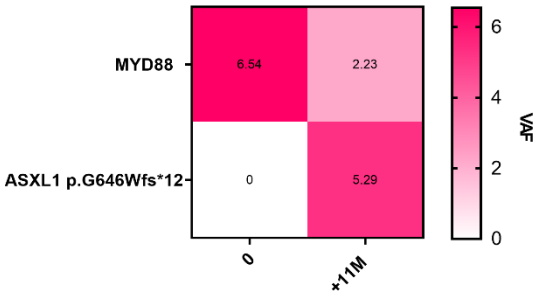
Treatment: +24M to Present Bendamustine and Rituximab

Patient ID #1647



Treatment: 0 to 20M Rituximab, +23M to +27M Bortezomib and Dexamethason,+28M to +31M Umbralisib, +35M to Present Zanubrutinib.

Patient ID #1679



Treatment: 0 to +3M Carfilzomib, Dexamethason and Ofatumumab, +5M to Present Ibrutinib

Figure S7. Mutational spectrum and characteristics of patients with Waldenström Macroglobulinemia and MDS and/or AML. (A) The total number of WM patients that develop MDS or AML harboring one or more mutations in each gene. (B) Clonal dynamics of detected mutations before and after therapy with bendamustine and rituximab in a WM patient that developed MDS. Values depicted in each square represent VAF. (C) Number of patients receiving therapy. D) Co-mutation plot showing mutations present in all 15 patients that develop MDS or AML; each column represents a single patient. The top row denotes the maximum VAF in each patient, with darker shades of pink indicating higher VAF. The bar graph on the right designates the proportion of the different mutation subtypes for each gene. *B(D)R: Bortezomib, dexamethasone, rituximab. C(D)R: cyclophosphamide, dexamethasone, rituximab.*

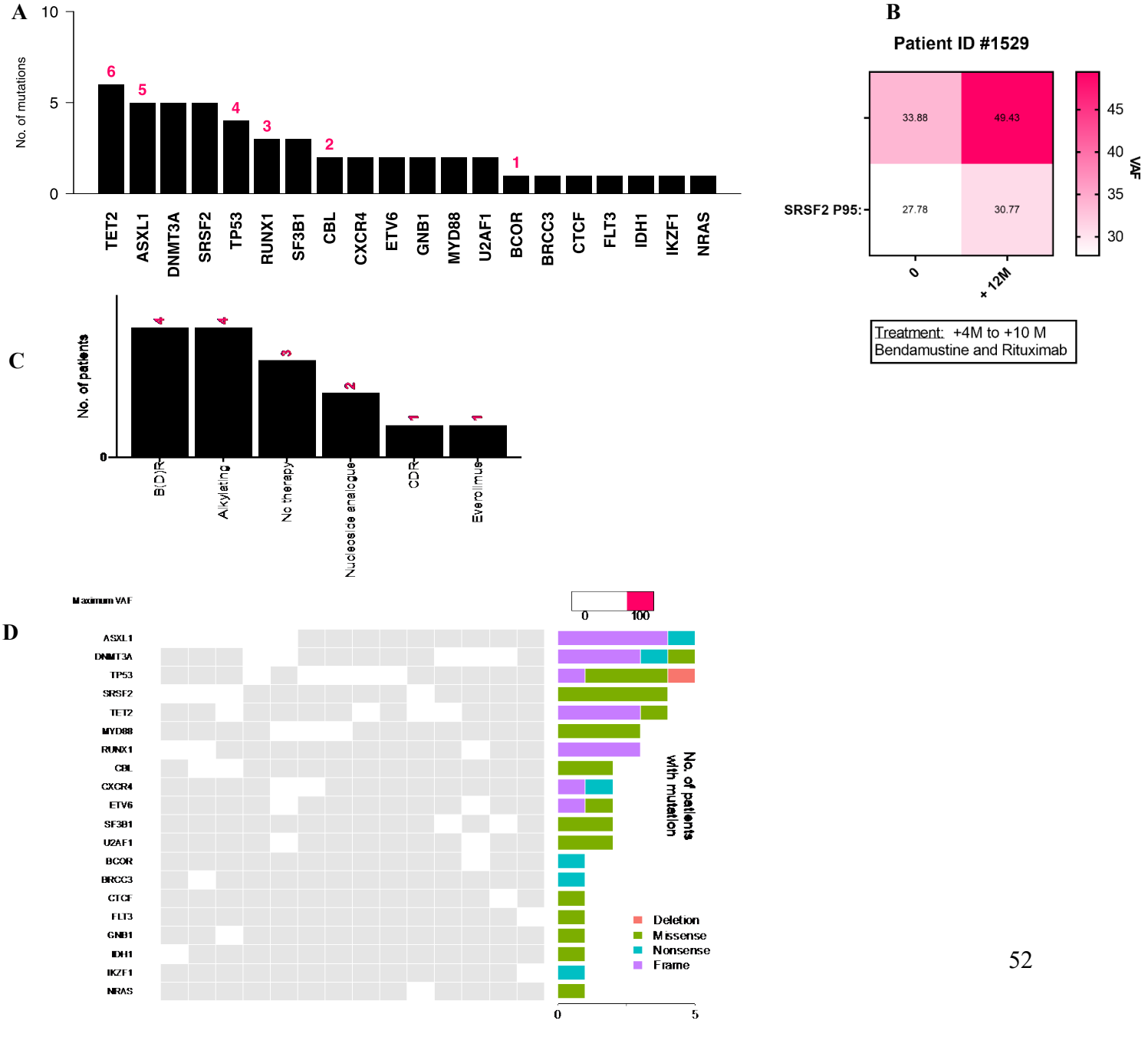


Figure S8. Mutational spectrum of CH in Waldenström Macroglobulinemia patients with *TP53* mutations. (A) OS and B) PFS among patients with *TP53* mutations versus those without *TP53* mutations from time of diagnosis. (C) Co-mutation plot showing mutations present in all 26 *TP53* mutated patients: each column represents a single patient. The top row denotes the maximum VAF in each patient, with darker shades of pink indicating higher VAF. The bar graph on the right designates the number of patients with a mutation detected in each gene.