SUPPLEMENTARY APPENDIX

Prognostic and predictive role of gene mutations in chronic lymphocytic leukemia: results from the pivotal phase III study COMPLEMENT1

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Supp. table 1:

Clinical and biological characteristics of full trial population of the complement 1 trial (n=447) and of the analysed cohort (n=383).

Patients	analysed cohort (n=383)	full trial (n=447)
Binet C	113 (29.5%)	139 (31.1%)
Male	246 (64.2%)	282 (63.1%)
B-Symtoms	214 (55.9%)	240 (53.7%)
IGHV	199 (52%)	226 (50.6%)
B2MG >5mg/l	168 (43.9%)	196 (43.8%)
del11q	58 (15.1%)	64 (14.3%)
del17p	19 (5%)	26 (5.8%)
Chl+O	183 (47.8%)	217 (48.5%)
ECOG>=1	142 (37.1%)	170 (38%)
Age =>75	96 (25.1%)	119 (26.6%)
CIRS>=8	236 (61.6%)	275 (61.5%)
WBC >50	226 (59%)	257 (57.5%)
CR rate	28 (7.3%)	30 (6.7%)
ORR	296 (77.3%)	336 (75.2%)
mPFS Clb (months)	12.8	13.1
mPFS O-Clb (months)	22.4	22.6

Supp. table 2:

Details of gene mutations identified in Complement1 including position dDNA and protein position, mutation type and variant frequency (VF).

SampleID	**Gene**	**Genomic description (hg19)**	**Protein description**	**type**	**VF**	*****
75644638	ATM	g.chr11:108098352A>T	p.M1L	missense	0.09	+
75624287	ATM	g.chr11:108099973C>G	p.S85*	nonsense	0.08	+
75623093	ATM	g.chr11:108115600C>T	p.R250*	nonsense	0.48	+
75622919	ATM	g.chr11:108117784A>G	p.Y332C	missense	0.80	+
75624010	ATM	g.chr11:108121532G>A	p.R447Q	missense	0.57	+
75624191	ATM	g.chr11:108129749C>T	p.R805*	nonsense	0.50	+
75642552	ATM	g.chr11:108137953A>C	p.D841A	missense	0.50	+
75624035	ATM	g.chr11:108138012T>A	p.Y861N	missense	0.50	+
75623126	ATM	g.chr11:108141874G>T	p.?	splice site	0.35	+
99293053	ATM	g.chr11:108141988T>C	p.S978P	missense	0.45	+
99294189	ATM	g.chr11:108143448G>A	p.?	splice site	0.15	+
99294528	ATM	g.chr11:108143467T>C	p.W1058R	missense	0.86	+
75645142	ATM	g.chr11:108143540A>G	p.H1082R	missense	0.64	+
75642181	ATM	g.chr11:108151768G>C	p.R1150T	missense	0.49	+
75622394	ATM	g.chr11:108155132G>A	p.A1309T	missense	0.89	+
99292938	ATM	g.chr11:108155132G>A	p.A1309T	missense	0.49	+
75623901	ATM	g.chr11:108168076G>C	p.A1658P	missense	0.36	+
99294308	ATM	g.chr11:108170477T>C	p.I1681T	missense	0.51	+
75623471	ATM	g.chr11:108170479G>T	p.D1682Y	missense	0.15	+
99294562	ATM	g.chr11:108170576T>A	p.M1714K	missense	0.61	+
75623218	ATM	g.chr11:108170588T>A	p.L1718Q	missense	0.11	+
75622916	ATM	g.chr11:108173578A>G	p.?	splice site	0.74	+
99295497	ATM	g.chr11:108175528C>T	p.R1875*	nonsense	0.08	+
75642992	ATM	g.chr11:108178641C>T	p.R1898*	nonsense	0.36	+
75623077	ATM	g.chr11:108183221T>A	p.L2001*	nonsense	0.92	+
75622394	ATM	g.chr11:108186598T>C	p.Y2019H	missense	0.64	+
75622837	ATM	g.chr11:108186740T>C	p.L2033P	missense	0.81	+
75621166	ATM	g.chr11:108186746C>A	p.T2035K	missense	0.86	+
99294655	ATM	g.chr11:108186757G>A	p.E2039K	missense	0.44	+
75622640	ATM	g.chr11:108190788A>C	p.?	splice site	0.45	+
99295579	ATM	g.chr11:108192066A>T	p.E2164V	missense	0.08	+
99294163	ATM	g.chr11:108196143C>T	p.R2227C	missense	0.38	+
75645227	ATM	g.chr11:108196851C>T	p.Q2292*	nonsense	0.40	+
75645303	ATM	g.chr11:108198427G>A	p.W2344*	nonsense	0.55	+
75623093	ATM	g.chr11:108198454C>T	p.P2353L	missense	0.43	+
75623899	ATM	g.chr11:108199837T>G	p.F2393L	missense	0.08	+
75623164	ATM	g.chr11:108199853C>T	p.Q2399*	nonsense	0.50	+

75623164	ATM	g.chr11:108200976A>T	p.D2448V	missense	0.14	+
75646539	ATM	g.chr11:108201081G>A	p.W2483*	nonsense	0.07	+
99293079	ATM	g.chr11:108201096G>A	p.C2488Y	missense	0.90	+
99295509	ATM	g.chr11:108206578G>A	p.D2720N	missense	0.80	+
75624191	ATM	g.chr11:108206581G>A	p.D2721N	missense	0.49	+
75623471	ATM	g.chr11:108216637T>A	p.?	splice site	0.19	+
75623214	ATM	g.chr11:108218089C>G	p.L2890V	missense	0.17	+
75622328	ATM	g.chr11:108225594T>C	p.I2948T	missense	0.95	+
75622804	ATM	g.chr11:108236086C>T	p.R3008C	missense	0.96	+
75642131	ATM	g.chr11:108236086C>T	p.R3008C	missense	0.83	+
99294189	ATM	g.chr11:108236087G>A	p.R3008H	missense	0.14	+
75643260	ATM	g.chr11:108236087G>A	p.R3008H	missense	0.14	+
75623078	ATM	g.chr11:108236096T>A	p.M3011K	missense	0.08	+
99295520	ATM	g.chr11:108236213C>T	p.P3050L	missense	0.51	+
99295580	BIRC3	g.chr11:102199674C>A	p.S360*	nonsense	0.09	
75622837	BIRC3	g.chr11:102201909_102201910del1	p.F421fs	frame_shift_del	0.53	
75622919	BIRC3	g.chr11:102201945G>T	p.E433*	nonsense	0.71	
75623222	BIRC3	g.chr11:102201970C>G	p.S441*	nonsense	0.13	
75623329	BIRC3	g.chr11:102206695A>G	p.?	splice site	0.44	
75623997	BIRC3	g.chr11:102206924G>A	p.E518K	missense	0.41	
75623222	BIRC3	g.chr11:102207512T>G	p.I534S	missense	0.07	
75623222	BIRC3	g.chr11:102207518C>G	p.T536R	missense	0.14	
75623222	BIRC3	g.chr11:102207523G>T	p.D538Y	missense	0.14	
99295329	BIRC3	g.chr11:102207651G>T	p.E545*	nonsense	0.43	
99295580	BIRC3	g.chr11:102207656_102207657del1	p.D546fs	frame_shift_del	0.44	
75642984	BIRC3	g.chr11:102207697G>A	p.C560Y	missense	0.68	
99294283	BIRC3	g.chr11:102207756G>T	p.D580Y	missense	0.54	
75642575	FBXW7	g.chr4:153244303T>C	p.?	splice site	0.45	+
99294628	FBXW7	g.chr4:153247171A>G	p.V544A	missense	0.20	+
75622951	FBXW7	g.chr4:153247294G>A	p.A503V	missense	0.47	+
99295316	FBXW7	g.chr4:153247366C>T	p.R479Q	missense	0.10	+
99294721	FBXW7	g.chr4:153247366C>A	p.R479Q	missense	0.39	+
75622630	FBXW7	g.chr4:153249384C>T	p.R465H	missense	0.32	+
75623209	FBXW7	g.chr4:153249385G>A	p.R465C	missense	0.39	+
99295202	FBXW7	g.chr4:153249385G>A	p.R465C	missense	0.32	+
75646433	FBXW7	g.chr4:153249504C>A	p.W425L	missense	0.35	+
75623502	FBXW7	g.chr4:153268222T>C	p.T196A	missense	0.43	+
75623981	FBXW7	g.chr4:153332910_153332911_ins3	p.G16A	in_frame_ins	0.46	+
75623579	FBXW7	g.chr4:153244092G>A	p.R689W	missense	0.41	+
75642984	FBXW7	g.chr4:153244229T>A	p.D643V	missense	0.47	+
75642984	FBXW7	g.chr4:153244268A>C	p.L630*	nonsense	0.55	+
99294139	MYD88	g.chr3:38182025G>T	p.V217F	missense	0.32	
75623281	MYD88	g.chr3:38182025G>T	p.V217F	missense	0.44	
75621191	MYD88	g.chr3:38182025G>T	p.V217F	missense	0.34	

99295172	MYD88	g.chr3:38182025G>T	p.V217F	missense	0.26	
75623203	MYD88	g.chr3:38182032C>G	p.S219C	missense	0.20	
99294344	MYD88	g.chr3:38182032C>G	p.S219C	missense	0.32	
99293452	MYD88	g.chr3:38182032C>G	p.S219C	missense	0.26	
75622905	MYD88	g.chr3:38182641T>C	p.L265P	missense	0.16	
75622516	MYD88	g.chr3:38182641T>C	p.L265P	missense	0.42	
75622670	MYD88	g.chr3:38182641T>C	p.L265P	missense	0.40	
75646539	NOTCH1	g.chr9:139,390,145T>C	p.?	3'UTR	-	
99294652	NOTCH1	g.chr9:139,390,145T>C	p.?	3'UTR	-	
75623165	NOTCH1	g.chr9:139,390,152T>C	p.?	3'UTR	-	
99295184	NOTCH1	g.chr9:139,390,152T>C	p.?	3'UTR	-	
75624112	NOTCH1	g.chr9:139,390,152T>C	p.?	3'UTR	-	
75623454	NOTCH1	g.chr9:139,390,152T>C	p.?	3'UTR	-	
75622399	NOTCH1	g.chr9:139,390,152T>C	p.?	3'UTR	-	
99293071	NOTCH1	g.chr9:139,390,152T>C	p.?	3'UTR	-	
75622956	NOTCH1	g.chr9:139,390,152T>C	p.?	3'UTR	-	
75623471	NOTCH1	g.chr9:139,390,152T>C	p.?	3'UTR	-	
99295452	NOTCH1	g.chr9:139,390,152T>C	p.?	3'UTR	-	
99295329	NOTCH1	g.chr9:139,390,152T>C	p.?	3'UTR	-	
99295163	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.12	+
75622435	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.1	+
75622440	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.09	+
75623050	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.24	+
75623126	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.25	+
75623230	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.47	+
75624585	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.2	+
99294423	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.47	+
75622317	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.53	+
75622346	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.32	+
75623188	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.47	+
75623189	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.48	+
75623997	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.19	+
75623998	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.49	+
99293603	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.2	+
99294365	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.48	+
75622829	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.26	+
75622916	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.06	+
99293238	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.31	+
99294447	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.31	+
99295329	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.07	+
99295564	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.49	+
75622598	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.42	+
75622863	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.77	+
75623236	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.44	+

75623981	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.27	+
75624243	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.06	+
99293053	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.14	+
20203767	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.64	+
75622811	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.58	+
75623048	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.3	+
75623329	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.4	+
75623471	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.16	+
99292938	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.43	+
99295520	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.06	+
75623089	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.43	+
75642432	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.38	+
75645239	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.37	+
75645261	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.39	+
75646485	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.37	+
75646531	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.48	+
75646539	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.37	+
99293108	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.39	+
75623186	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.35	+
75623502	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.4	+
99294164	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.43	+
99293038	NOTCH1	g.chr9:139390649_139390650del2	p.P2514fs	frame_shift_del	0.07	+
99295580	NOTCH1	g.chr9:139390780_139390781del1	p.P2471fs	frame_shift_del	0.41	+
99294528	NOTCH1	g.chr9:139390861G>A	p.Q2444*	nonsense	0.45	+
99293241	NOTCH1	g.chr9:139390945G>A	p.Q2416*	nonsense	0.54	+
75622429	NOTCH1	g.chr9:139390966G>A	p.Q2409*	nonsense	0.31	+
75623901	NOTCH1	g.chr9:139390981G>A	p.Q2404*	nonsense	0.08	+
75624612	NOTCH1	g.chr9:139391011G>A	p.Q2394*	nonsense	0.85	+
75622857	NOTCH1	g.chr9:139391272G>A	p.Q2307*	nonsense	0.83	+
75623054	NOTCH1	g.chr9:139391442G>A	p.A2250V	missense	0.59	
75646512	NOTCH1	g.chr9:139391629C>T	p.G2188S	missense	0.52	
75620687	POT1	g.chr7:124475458_124475460del2	p.L460fs	frame_shift_del	0.52	
99293603	POT1	g.chr7:124481141A>T	p.Y419N	missense	0.48	
75646555	POT1	g.chr7:124482894G>A	p.S377F	missense	0.51	
75623054	POT1	g.chr7:124482937G>A	p.R363*	nonsense	0.49	
99293084	POT1	g.chr7:124493042C>A	p.V285L	missense	0.32	
75622733	POT1	g.chr7:124493075C>T	p.G274R	missense	0.35	
75622310	POT1	g.chr7:124493077C>T	p.R273Q	missense	0.11	
75622361	POT1	g.chr7:124493077C>T	p.R273Q	missense	0.22	
99294362	POT1	g.chr7:124493098T>G	p.H266P	missense	0.41	
75622572	POT1	g.chr7:124493142C>A	p.M251I	missense	0.49	
99294139	POT1	g.chr7:124493167C>A	p.S243I	missense	0.34	
99293452	POT1	g.chr7:124493170T>C	p.Y242C	missense	0.26	
75623502	POT1	g.chr7:124499036T>A	p.H226L	missense	0.37	

99294652	POT1	g.chr7:124499043C>T	p.D224N	missense	0.47	
99293060	POT1	g.chr7:124503519A>G	p.M144T	missense	0.48	
99295531	POT1	g.chr7:124503636G>A	p.T105M	missense	0.46	
75623400	POT1	g.chr7:124503682T>C	p.K90E	missense	0.46	
99292358	POT1	g.chr7:124503687A>G	p.V88A	missense	0.49	
99293371	POT1	g.chr7:124510963A>G	p.?	splice site	0.14	
99293416	POT1	g.chr7:124510966T>C	p.K85R	missense	0.49	
75646555	POT1	g.chr7:124510987A>G	p.I78T	missense	0.48	
99295184	POT1	g.chr7:124511014A>C	p.L69R	missense	0.40	
75624035	POT1	g.chr7:124511080A>T	p.V47E	missense	0.31	
75645174	POT1	g.chr7:124511096C>A	p.?	splice site	0.34	
99293038	POT1	g.chr7:124532329T>C	p.K39E	missense	0.46	
75622429	POT1	g.chr7:124532330G>C	p.S38R	missense	0.32	
99293238	POT1	g.chr7:124532393_124532394del1	p.L17fs	frame_shift_del	0.38	
75623997	POT1	g.chr7:124532398G>A	p.Q16*	nonsense	0.10	
75622435	POT1	g.chr7:124537227T>C	p.M1V	missense	0.33	
75623998	POT1	g.chr7:124537227T>C	p.M1V	missense	0.49	
75622611	POT1	g.chr7:124537267C>A	p.?	splice site	0.38	
0075622402	RPS15	g.chr19:1440414C>T	P131S	missense	-	
0075642392	RPS15	g.chr19:1440414C>T	P131S	missense	-	
0075623579	RPS15	g.chr19:1440415C>T	P131L	missense	-	
0075623228	RPS15	g.chr19:1440417G>T	G132C	missense	-	
0075622390	RPS15	g.chr19:1440424G>C	G134A	missense	-	
0075642540	RPS15	g.chr19:1440427C>G	A135G	missense	-	
0075622647	RPS15	g.chr19:1440429A>G	T136A	missense	-	
0099294365	RPS15	g.chr19:1440432C>T	H137Y	missense	-	
0075623997	RPS15	g.chr19:1440432C>T	H137Y	missense	-	
0099294308	RPS15	g.chr19:1440436C>T	S138F	missense	-	
0099293452	RPS15	g.chr19:1440436C>T	S138F	missense	-	
0075623165	RPS15	g.chr19:1440436C>T	S138F	missense	-	
0099294271	RPS15	g.chr19:1440439C>T	S139F	missense	-	
0099293370	RPS15	g.chr19:1440439C>T	S139F	missense	-	
0075645275	RPS15	g.chr19:1440456A>C	K145Q	missense	-	
0020203710	RPS15	g.chr19:1440457_1440446del12	p.?	nonsense	-	
0075623223	RPS15	g.chr19:1440458G>C	K145N	missense	-	
99293347	SF3B1	g.chr2:198265474C>G	p.G895R	missense	0.33	
75645830	SF3B1	g.chr2:198265593T>C	p.D855G	missense	0.32	
75623185	SF3B1	g.chr2:198266488T>C	p.E783G	missense	0.4	
75623267	SF3B1	g.chr2:198266512C>T	p.R775Q	missense	0.12	
75624045	SF3B1	g.chr2:198266512C>T	p.R775Q	missense	0.26	
75643260	SF3B1	g.chr2:198266611C>T	p.G742D	missense	0.1	
75622310	SF3B1	g.chr2:198266611C>T	p.G742D	missense	0.14	
99293452	SF3B1	g.chr2:198266611C>T	p.G742D	missense	0.16	
75623981	SF3B1	g.chr2:198266611C>T	p.G742D	missense	0.18	

99295452	SF3B1	g.chr2:198266611C>T	p.G742D	missense	0.26	
75624222	SF3B1	g.chr2:198266611C>T	p.G742D	missense	0.3	
99293108	SF3B1	g.chr2:198266611C>T	p.G742D	missense	0.36	
99292900	SF3B1	g.chr2:198266611C>T	p.G742D	missense	0.41	
75622635	SF3B1	g.chr2:198266611C>T	p.G742D	missense	0.43	
99295600	SF3B1	g.chr2:198266611C>T	p.G742D	missense	0.45	
75623078	SF3B1	g.chr2:198266709C>A	p.K741N	missense	0.08	
75624616	SF3B1	g.chr2:198266713C>T	p.G740E	missense	0.08	
75624045	SF3B1	g.chr2:198266821A>T	p.I704N	missense	0.16	
99293370	SF3B1	g.chr2:198266822T>A	p.I704F	missense	0.29	
99294344	SF3B1	g.chr2:198266822T>A	p.I704F	missense	0.38	
99295168	SF3B1	g.chr2:198266824G>A	p.T703I	missense	0.4	
75624174	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.07	
99294652	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.08	
75624616	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.09	
75645300	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.09	
99294189	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.16	
75622479	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.21	
75644240	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.32	
75644614	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.41	
75623833	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.41	
75623400	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.42	
75623661	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.43	
99293084	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.43	
75623297	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.46	
75646555	SF3B1	g.chr2:198266834T>C	p.K700E	missense	0.47	
75624222	SF3B1	g.chr2:198267359C>G	p.K666N	missense	0.08	
75623584	SF3B1	g.chr2:198267359C>G	p.K666N	missense	0.18	
99294163	SF3B1	g.chr2:198267360T>G	p.K666T	missense	0.31	
99295436	SF3B1	g.chr2:198267360T>G	p.K666T	missense	0.43	
99294563	SF3B1	g.chr2:198267360T>G	p.K666T	missense	0.46	
75623232	SF3B1	g.chr2:198267361T>C	p.K666E	missense	0.43	
99295506	SF3B1	g.chr2:198267369G>A	p.T663I	missense	0.37	
75622733	SF3B1	g.chr2:198267369G>A	p.T663I	missense	0.35	
75622414	SF3B1	g.chr2:198267373G>C	p.H662D	missense	0.46	
75645142	SF3B1	g.chr2:198267373>C	p.H662D	missense	0.39	
99293079	SF3B1	g.chr2:198267480T>C	p.N626S	missense	0.14	
75642131	SF3B1	g.chr2:198267480T>C	p.N626S	missense	0.25	
75624272	SF3B1	g.chr2:198267481T>A	p.N626Y	missense	0.45	
99294338	SF3B1	g.chr2:198267483C>A	p.R625L	missense	0.28	
75645828	SF3B1	g.chr2:198267483C>T	p.R625H	missense	0.44	
75623308	SF3B1	g.chr2:198267489T>C	p.Y623C	missense	0.16	
99293540	SF3B1	g.chr2:198267489T>C	p.Y623C	missense	0.12	
75624601	SF3B1	g.chr2:198267489T>C	p.Y623C	missense	0.4	

75620663	SF3B1	g.chr2:198267489T>C	p.Y623C	missense	0.17	
99295497	SF3B1	g.chr2:198267491C>A	p.E622D	missense	0.47	
99294655	SF3B1	g.chr2:198267498A>T	p.M620K	missense	0.33	
99295560	SF3B1	g.chr2:198267510T>A	p.D616V	missense	0.44	
75623061	TP53	g.chr17:7572958A>G	p.M384T	missense	0.54	
75623454	TP53	g.chr17:7572989C>G	p.G374R	missense	0.38	
99294164	TP53	g.chr17:7576919_7576919del1	p.P309fs	frame_shift_del	0.44	
75623118	TP53	g.chr17:7577079_7577093del15	p.R282Q	in_frame_del	0.88	
99293065	TP53	g.chr17:7577093_7577094ins8	p.R282fs	frame_shift_del	0.87	
75623957	TP53	g.chr17:7577091G>A	p.R283C	missense	0.41	
75623013	TP53	g.chr17:7577095G>C	p.D281E	missense	0.13	
75622951	TP53	g.chr17:7577096T>C	p.D281G	missense	0.92	
75623508	TP53	g.chr17:7577096T>C	p.D281G	missense	0.60	
75622956	TP53	g.chr17:7577100T>C	p.R280G	missense	0.28	
75646538	TP53	g.chr17:7577111G>T	p.A276D	missense	0.08	
99294710	TP53	g.chr17:7577124C>T	p.V272M	missense	0.45	
75624272	TP53	g.chr17:7577498C>T	p.?	splice site	0.77	
99294721	TP53	g.chr17:7577506C>A	p.D259Y	missense	0.84	
75622743	TP53	g.chr17:7577539G>A	p.R248W	missense	0.44	
99294271	TP53	g.chr17:7577565T>C	p.N239S	missense	0.49	
75623530	TP53	g.chr17:7577570C>T	p.M237I	missense	0.15	
75623210	TP53	g.chr17:7578190T>C	p.Y220C	missense	0.71	
99294283	TP53	g.chr17:7578206T>C	p.S215G	missense	0.64	
75623443	TP53	g.chr17:7578222_7578223del2	p.?	nonsense	0.66	
75622975	TP53	g.chr17:7578244C>G	p.R202P	missense	0.51	
99294164	TP53	g.chr17:7578262C>G	p.R196P	missense	0.43	
99294710	TP53	g.chr17:7578263G>A	p.R196*	nonsense	0.42	
75623165	TP53	g.chr17:7578394T>C	p.H179R	missense	0.20	
75623223	TP53	g.chr17:7578394T>C	p.H179R	missense	0.39	
75622741	TP53	g.chr17:7578394T>C	p.H179R	missense	0.32	
99295302	TP53	g.chr17:7578395G>A	p.H179Y	missense	0.79	
75642130	TP53	g.chr17:7578457C>T	p.R158H	missense	0.28	
75623209	TP53	g.chr17:7578490_7578491ins2	p.V147fs	frame-shift-ins	0.81	
20203756	TP53	g.chr17:7578490A>T	p.V147D	missense	0.61	
75623209	TP53	g.chr17:7578494_7578491ins2	p.W147fs	frame-shift-ins	0.05	
75622414	TP53	g.chr17:7578517G>A	p.A138V	missense	0.86	
75622647	TP53	g.chr17:7578535T>C	p.K132R	missense	0.82	
99293008	TP53	g.chr17:7579350A>C	p.F113V	missense	0.79	
75624010	TP53	g.chr17:7579377G>A	p.Q104*	nonsense	0.74	
99295331	TP53	g.chr17:7579528C>T	p.W53*	nonsense	0.89	
99294565	TP53	g.chr17:7577538C>T	p.R248Q	missense	0.86	
75646563	TP53	g.chr17:7577106A>A	p.R278S	missense	0.96	
75622863	TP53	g.chr17:7577550C>T	p.G244D	missense	0.39	
99293540	TP53	g.chr17:7577120C>T	p.R273H	missense	0.18	

75641558	TP53	g.chr17:7577120C>A	p.R273L	missense	0.84	
75622402	TP53	g.chr17:7578406C>T	p.R175H	missense	0.29	
99293540	TP53	g.chr17:7578479G>A	p.P151S	missense	0.16	

Supp. table3:

Associations of clinical, laboratory and genetic parameters with gene mutations. Incidences, odds ratio and p value is given for presence vs. absence of each parameter.

	TP53			SF3B1			NOTCH1			ATM			RPS15		
Parameter	Incidence	Odds ratio	p	Incidence	Incidence	Incidence	Incidence	Odds ratio	p	Incidence	Odds ratio	P	Incidence	Odds ratio	P
Male sex	9% vs. 12%	0.78	0.48	**17% vs. 9%**	**2.14**	**0.03**	17% vs. 28%	0.59	0.06	16% vs. 9%	1.83	0.1	5% vs. 4%	1.83	0.1
Age >70y	13% vs. 8%	1.86	0.09	13% vs. 16%	0.78	0.46	18% vs. 22%	0.82	0.55	12% vs. 14%	0.86	0.75	3% vs. 6%	0.44	0.14
Binet C	14% vs. 9%	1.77	0.1	17% vs. 13%	1.36	0.34	24% vs. 18%	1.29	0.41	11% vs. 14%	0.75	0.49	6% vs. 4%	1.32	0.59
Splenomegaly	9% vs. 6%	1.55	0.4	16% vs. 13%	1.27	0.51	24% vs. 17%	1.46	0.28	15% vs. 11%	1.47	0.37	5% vs. 3%	1.61	0.57
Bone marrow infiltrate	10% vs. 10%	0.98	1	14% vs. 14%	1.04	1	0% vs. 21%	-	-	11% vs. 21%	0.54	0.09	5% vs. 4%	1.39	0.77
B-symptoms	9% vs. 11%	0.81	0.61	16% vs. 11%	1.54	0.18	20% vs. 22%	0.91	0.78	15% vs. 11%	1.34	0.43	4% vs. 5%	0.88	0.81
high b2MG	**14% vs. 6%**	**2.49**	**0.01**	17% vs. 12%	1.46	0.23	**11% vs. 30%**	**0.38**	**<0.01**	15% vs. 12%	1.21	0.63	5% vs. 5%	0.9	1
WBC >50G/L	**11% vs. 5%**	**2.59**	**0.05**	16% vs. 10%	1.72	0.15	24% vs. 14%	1.74	0.08	**18% vs. 8%**	**2.21**	**0.03**	**7% vs. 0%**	**-**	**<0.01**
CIRS≥8	10% vs. 10%	1	1	14% vs. 14%	1.07	0.88	22% vs. 18%	1.27	0.48	13% vs. 13%	1.03	1	5% vs. 4%	1.15	1
IGHV unmutated	**13% vs. 6%**	**2.17**	**0.05**	16% vs. 12%	1.39	0.36	23% vs. 12%	2.01	0.13	18% vs. 9%	1.95	0.07	**8.5% vs. 0%**	**-**	**p<0.01**
del11q	3% vs. 11%	0.28	0.09	19% vs. 13%	1.51	0.31	19% vs. 25%	0.77	0.75	**53% vs. 8%**	**6.58**	**<0.01**	5% vs. 5%	1.16	0.74
del13q	12% vs. 7%	1.81	0.12	12% vs. 17%	0.7	0.24	15% vs. 30%	0.48	0.01	14% vs. 13%	1.09	0.87	6% vs. 4%	1.78	0.32
del17p	**89% vs. 6%**	**136**	**<0.01**	0% vs. 15%	-	0.09	6% vs. 22%	0.25	0.22	0% vs. 14%	-	0.15	12% vs. 4%	2.64	0.21
+12q	**2% vs. 11%**	**0.14**	**0.03**	5% vs. 16%	0.31	0.06	41% vs. 18%	2.24	0.02	8% vs. 14%	0.54	0.37	5% vs. 2%	2.86	0.49
del6q	25% vs. 10%	3.05	0.34	0% vs. 14	-	-	**0% vs. 22%**	**-**	**-**	0% vs. 14%	-	-	33% vs. 5%	7.22	0.17

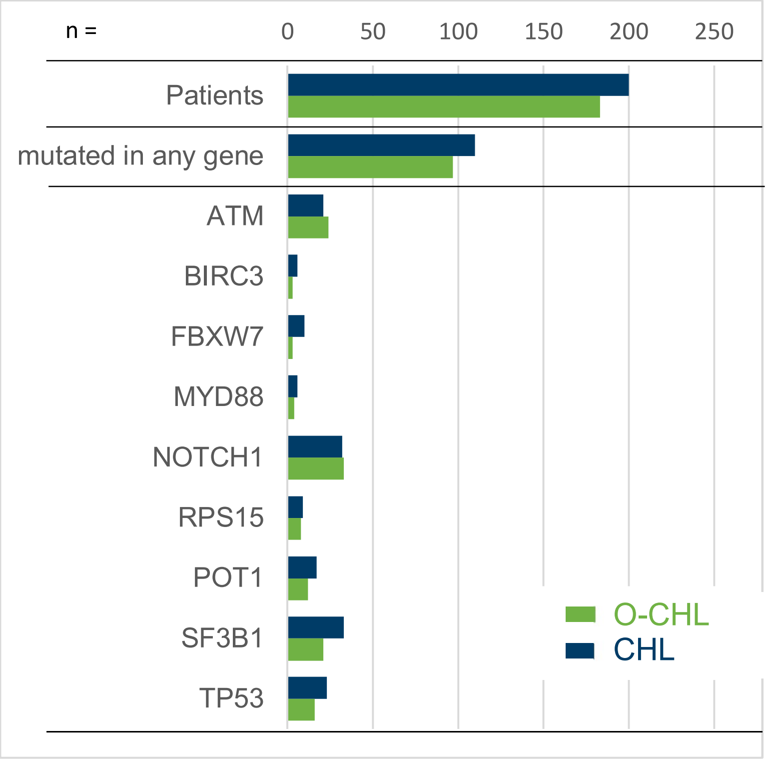
	POT1			BIRC3			MYD88			FBXW7		
Parameter	Incidence	Odds ratio	p	Incidence	Odds ratio	p	Incidence	Odds ratio	p	Incidence	Odds ratio	p
Male	8% vs. 9%	0.9	0.84	3% vs. 2%	1.12	1	3% vs. 2%	1.31	1	4% vs. 3%	1.26	0.78
Age >70y	9% vs. 8%	1.19	0.7	2% vs. 3%	0.54	0.51	2% vs. 3%	0.72	0.75	4% vs. 3%	1.29	0.78
Binet C	9% vs. 8%	1.08	0.83	2% vs. 3%	0.68	1	4% vs. 2%	2.45	0.17	4% vs. 3%	1.06	1
Splenomegaly	8% vs. 7%	1.25	0.66	2% vs. 2%	1.06	1	4% vs. 2%	2.89	0.2	3% vs. 2%	2.15	0.48
Bone marrow infiltrate	8% vs. 7%	1.14	1	2% vs. 2%	1.03	1	3% vs. 2%	1.18	1	3% vs. 5%	0.65	0.5
B-symptoms	10% vs. 6%	1.55	0.33	3% vs. 1%	2.82	0.31	2% vs. 4%	0.52	0.35	3% vs. 4%	0.67	0.57
high b2MG	11% vs. 7%	1.58	0.25	3% vs. 2%	1.56	0.52	2% vs. 2%	0.99	1	4% vs. 3%	1.46	0.58
WBC >50G/L	9% vs. 8%	1.05	1	3% vs. 1%	4.14	0.27	1% vs. 4%	0.23	0.11	4% vs. 2%	1.77	0.55
CIRS≥8	9% vs. 7%	1.42	0.43	3% vs. 1%	2.21	0.49	2% vs. 4%	0.41	0.19	4% vs. 2%	2.12	0.39
IGHV unmutated	11% vs. 6%	1.72	0.24	**5% vs. 0%**	-	**0.01**	**1% vs. 4%**	**0.11**	**0.02**	4% vs. 4%	0.91	1
del11q	5% vs. 9%	0.63	0.59	**12% vs. 1%**	**11.79**	**<0.01**	2% vs. 3%	0.67	1	2% vs. 4%	0.44	0.7
del13q	7% vs. 10%	0.75	0.56	2% vs. 3%	0.65	0.74	3% vs. 1%	2.94	0.19	2% vs. 5%	0.35	0.09
del17p	0% vs. 9%	-	0.38	6% vs. 2%	2.39	0.38	0% vs. 3%	-	1	**16% vs. 3%**	**6.36**	**0.02**
+12q	4% vs. 9%	0.41	0.28	**8% vs. 2%**	**4.86**	**0.03**	2% vs. 3%	0.71	1	**11% vs. 2%**	**5.26**	**0.01**
del6q	0% vs. 9%	-	-	0% vs. 3%	-	1	0% vs. 2%	-	1	0% vs.0%	0	1

Supp. table4:

Multivariate analysis for interaction of treatment and biomarker. Therefore the treatment arm, the mutated gene and their interaction were included in the analysis , which was repeated for every gene. Result table shows the hazard ratio (HR), confidence interval (CI 95%) and p-value of the interaction, and therefore the predictive impact.

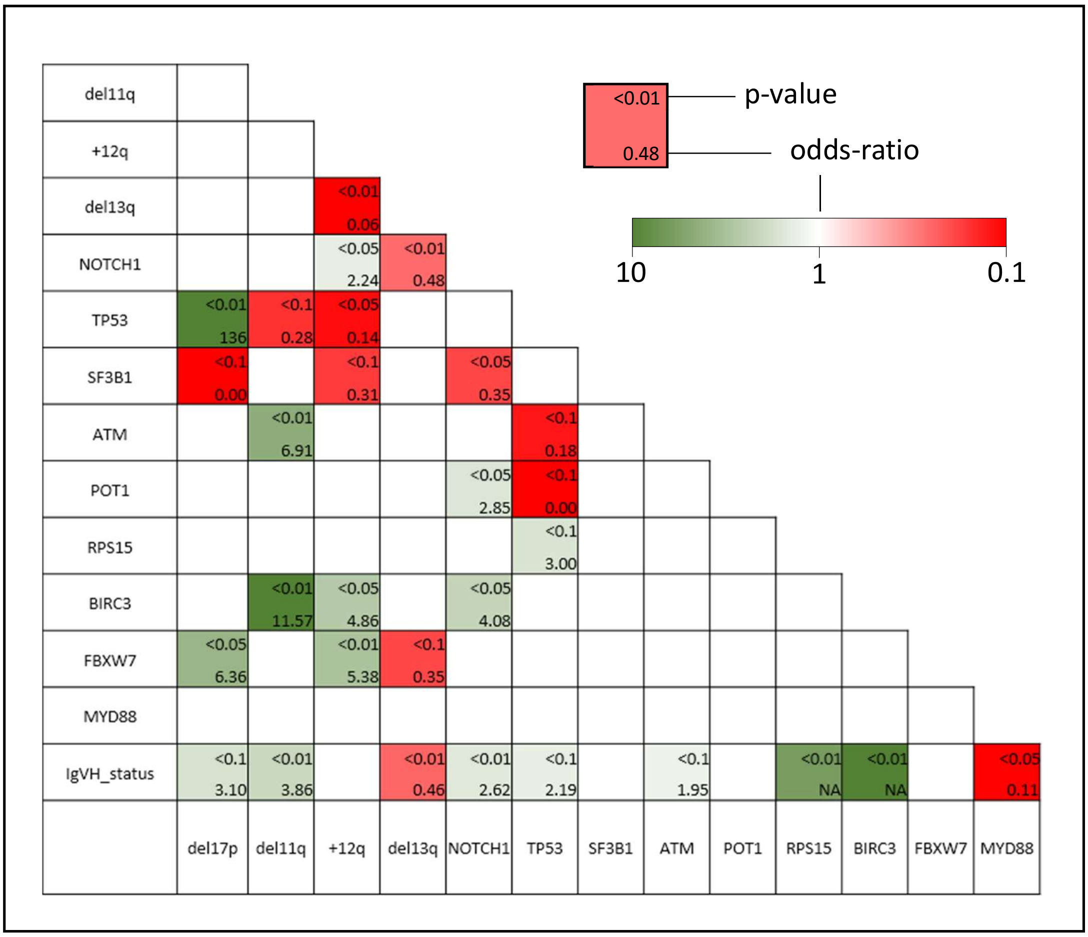
Gene	HR	CI 95%	p-value
TP53	0.77	0.34-1.74	0.53
NOTCH1	1.86	1-3.48	0.05
SF3B1	1.02	0.52-1.99	0.96
ATM	0.89	0.43-1.83	0.75
POT1	0.52	0.21-1.32	0.17
RPS15	0.94	0.27-3.33	0.92
FBXW7	0.93	0.19-4.55	0.92
MYD88	0.42	0.05-3.66	0.43
BIRC3	0.32	0.06-1.78	0.19

Supp. figure 1: Total numbers of patients and mutations subdivided into both treatment arms.



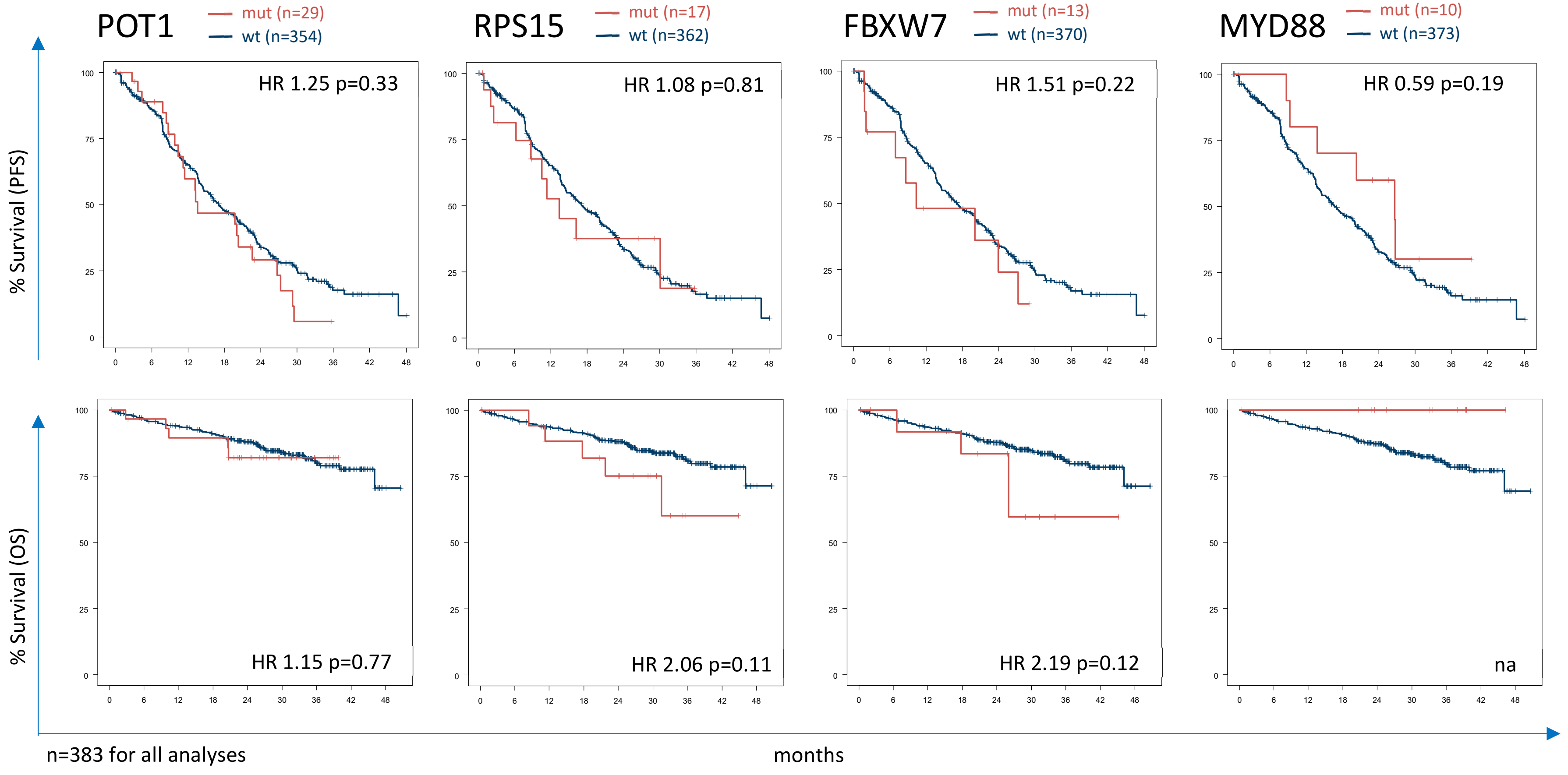
Supp. figure 2:

Associations of gene mutations and chromosomal aberrations considering false discovery rate (FDR). Numbers within the boxes show odd-ratio (lower right number in each box) and p-value categories (upper right number), which can be <0.1, <0.05 or <0.01. Green boxes represent significant co-occurrence (odds ratio >1), red box mutual exclusivity (odds ratio <1). For p-values >0.1, boxes remain bland and numbers are not provided.

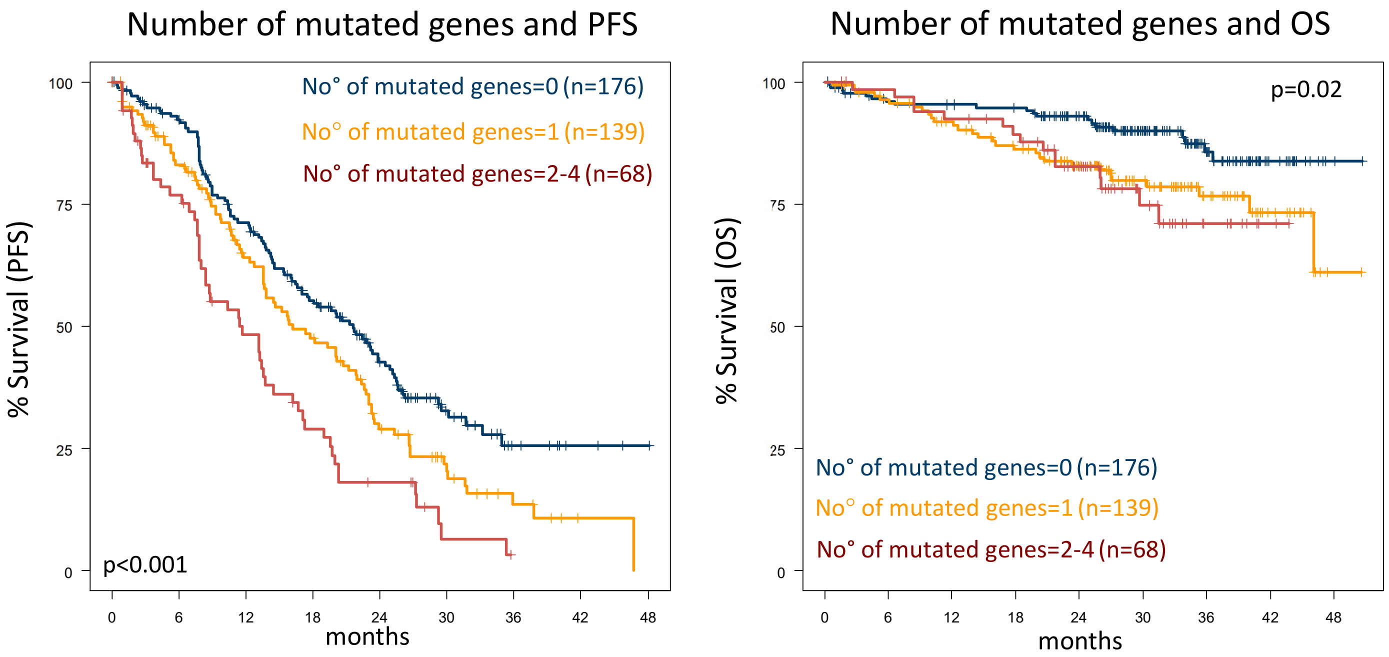


	del17p	del11q	+12q	del13q	NOTCH1	TP53	SF3B1	ATM	POT1	RPS15	BIRC3	FBXW7	MYD88
del11q													
+12q													
del13q			<0.01 0.06										
NOTCH1			<0.05 2.24	<0.01 0.48									
TP53	<0.01 136	<0.1 0.28	<0.05 0.14										
SF3B1	<0.1 0.00		<0.1 0.31		<0.05 0.35								
ATM		<0.01 6.91				<0.1 0.18							
POT1					<0.05 2.85	<0.1 0.00							
RPS15						<0.1 3.00							
BIRC3		<0.01 11.57	<0.05 4.86		<0.05 4.08								
FBXW7	<0.05 6.36		<0.01 5.38	<0.1 0.35									
MYD88													
IgVH_status	<0.1 3.10	<0.01 3.86		<0.01 0.46	<0.01 2.62	<0.1 2.19		<0.1 1.95		<0.01 NA	<0.01 NA		<0.05 0.11

Supp. figure 3: Kaplan-Meier estimates of PFS (top panels) and OS (bottom panels) according to the status of gene mutations in POT1, RPS15, FBXW7 and MYD88 for the total patient cohort. Mutated subgroups are depicted by red lines, and wild type by dark blue lines. Denoted P values were calculated by log-rank test (mutated vs. unmutated subgroup). Due to no events in OS of MYD88 mutated subgroup no odds ratio can be delineated.

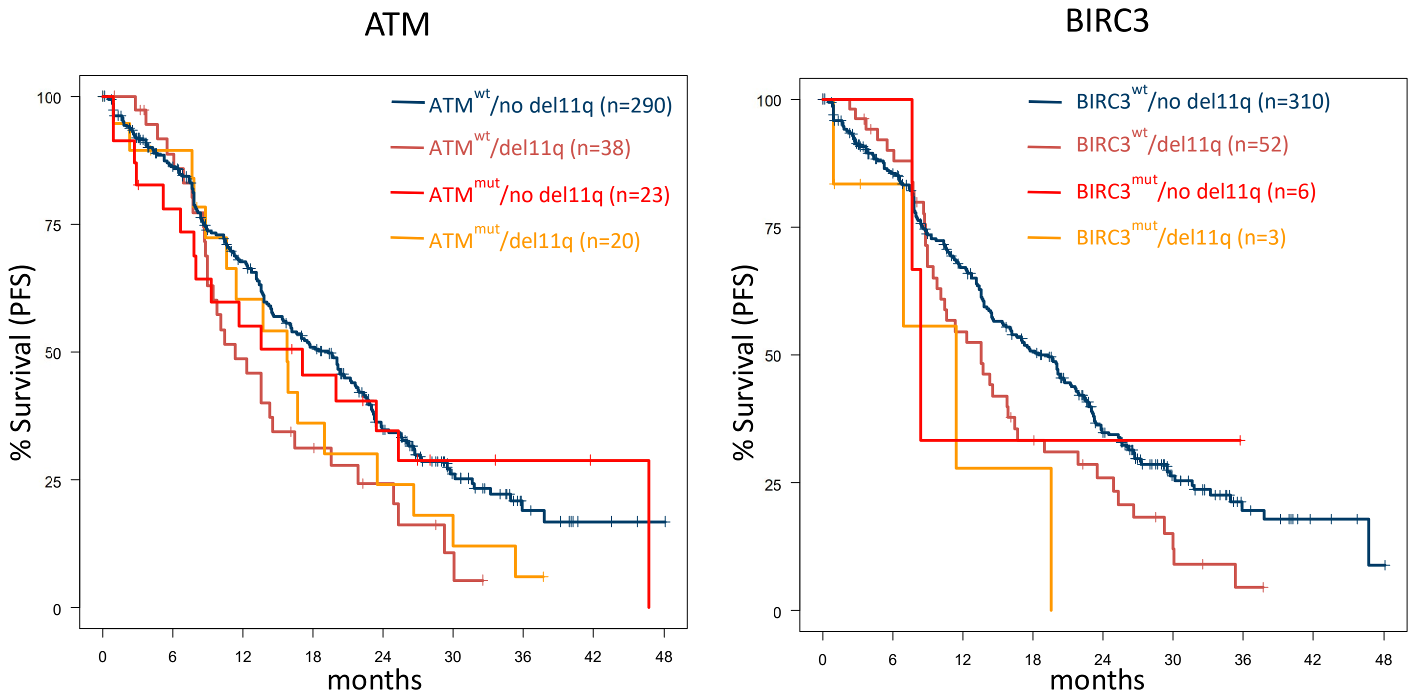


Supp. figure 4: Kaplan-Meier estimates of PFS (left) and OS (right) according to the number of mutated genes for the total patient cohort. Subgroups affected by 2 or more mutated genes are depicted by red lines, the subgroup with one mutated gene by yellow lines and wild type patients by dark blue lines. (n=383)

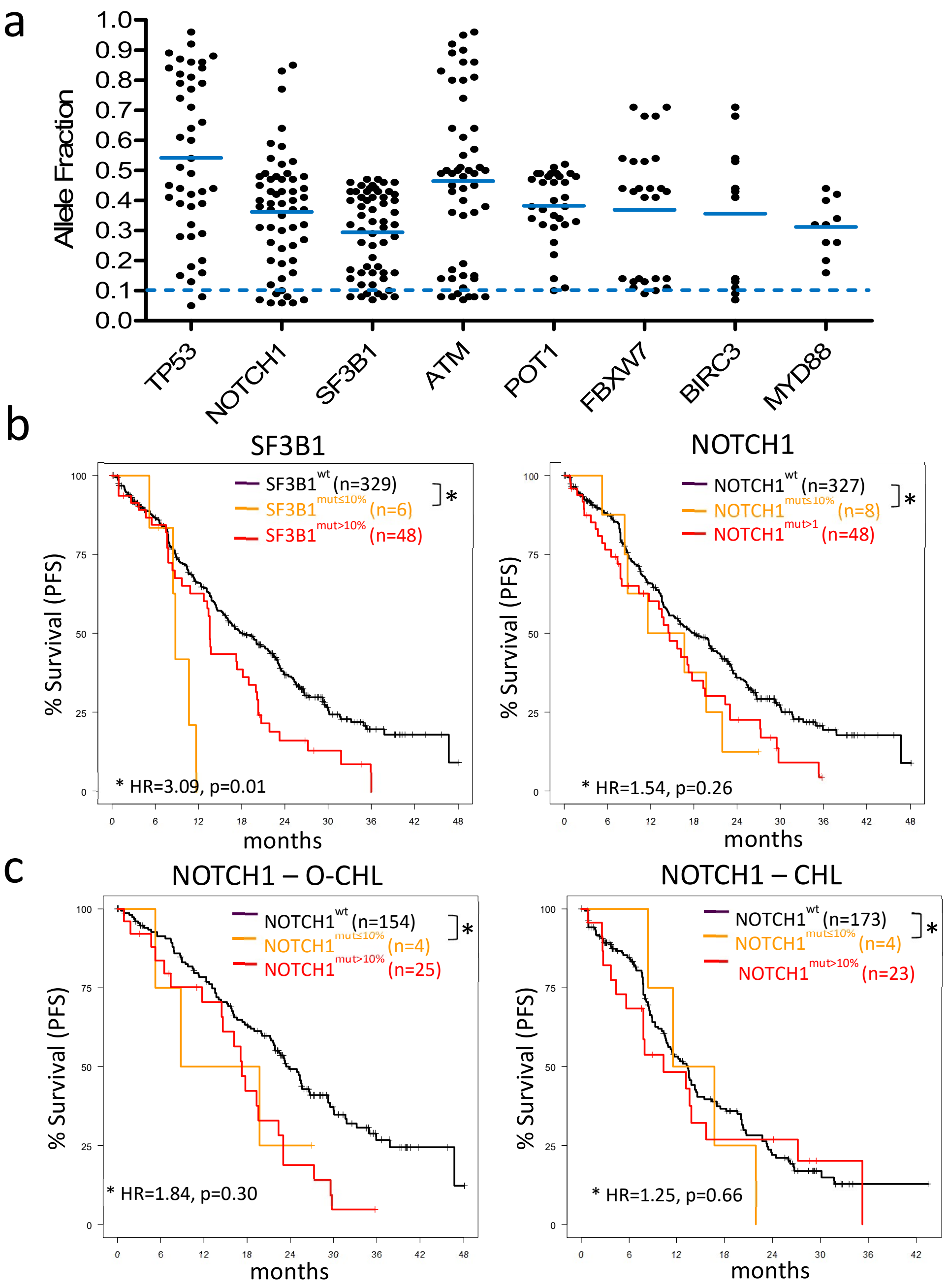

Number of mutated genes and PFS

Number of mutated genes and OS

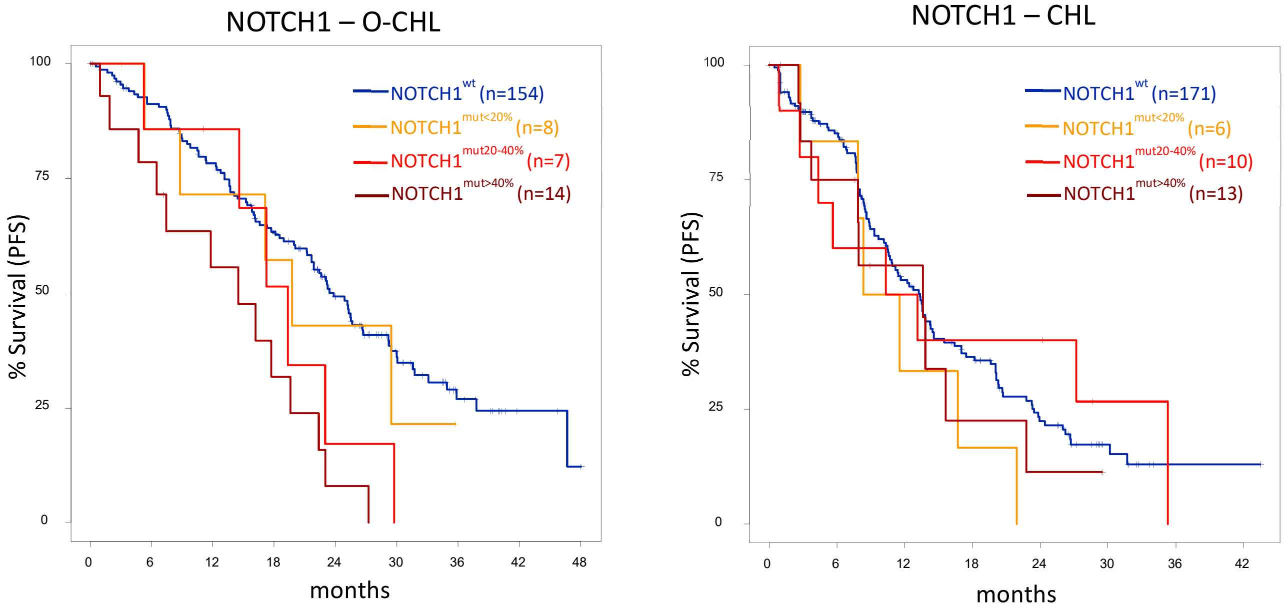
Supp. figure 5: Kaplan-Meier estimates of PFS for subgroups defined by *ATM* (left) and *BIRC3* (right) mutations and co-occurrence of 11q deletion. Mutation status is depicted by line color, 11q status by line structure. P value for log-rank (mutated vs. unmutated subgroup) is denoted for each subgroup.



Supp. figure 6) Allelic fraction of mutation within different genes. A) Each data point corresponds to the VAF of one patient, the lines depict mean allelic fractions within mutated subgroups. B) Kaplan-Meier estimates for PFS for *SF3B1* (left) and *NOTCH1* (right) mutations according to clone size (</> 10%VAF). Wildtype is coded blue, patients with only minor mutations (VAF<10%) in yellow, and patients with a major mutation (VAF>10%) in grey. 3'UTR mutations were not considered as the assessment via Sanger sequencing does not allow to detemine exact VAF and to detect minor variants.



Supp. figure 7) Kaplan-Meier estimates for PFS for *NOTCH1* mutations with different variant allele frequencies. For O-CHL treated patients major NOTCH1 mutations (>40% VAF) have short PFS, while with CHL therapy none of the NOTCH1 mutated subgroups associated with adverse outcome. 3'UTR mutations were not considered, as the assessment via Sanger sequencing does not allow detecting minor variants.



Supp. figure 8) Kaplan-Meier estimates for PFS (upper row) and OS (lower row) for mutated *TP53* (a), *SF3B1* (b), *NOTCH1* (c) and *NOTCH1* coding mutations with high allele frequency (“mut>40%coding) for O-CHL and CHL. For NOTCH1$^{mut>40\%coding}$ 3’UTR mutations were not considered as the assessment via Sanger sequencing does not allow to determine exact VAF.