

# HICF1 - Final Report v1

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## Univariate Analysis

Table 1: Univariate Analysis against MRD outcome

	p.value	uncorrected	corrected.p.value	corrected	MRDneg0	MRDpos1	MRDneg1	sum	testused
TP53_ALL	0.00004	***	0.002	**	105	19	2	209	Fisher's Exact Test
TP53_del	0.012	*	0.513	n.s.	107	6	0	209	Fisher's Exact Test
TP53_cnLOH	0.055	trend	1	n.s.	107	4	0	209	Fisher's Exact Test
TP53_mut	0.00001	***	0.001	***	107	15	0	209	Fisher's Exact Test
TP53_bi	0.009	**	0.360	n.s.	106	9	1	209	Fisher's Exact Test
ATM_ALL	0.002	**	0.085	trend	83	44	24	209	Fisher's Exact Test
ATM_mut	0.036	*	1	n.s.	88	31	19	209	Fisher's Exact Test
ATM_del	0.0005	***	0.022	*	98	28	9	209	Fisher's Exact Test
ATM_cnLOH	0.203	n.s.	1	n.s.	106	4	1	209	Fisher's Exact Test
ATM_mt1	1	n.s.	1	n.s.	101	5	6	209	Fisher's Exact Test
BIRC3_ALL	0.094	trend	1	n.s.	94	22	13	209	Fisher's Exact Test
BIRC3_mut	0.375	n.s.	1	n.s.	99	4	8	209	Fisher's Exact Test
BIRC3_del	0.002	**	0.076	trend	101	21	6	209	Fisher's Exact Test
ATM_bi	0.002	**	0.088	trend	102	19	5	209	Fisher's Exact Test
BIRC3_bi	0.360	n.s.	1	n.s.	106	3	1	209	Fisher's Exact Test
X11q_mono	0.046	*	1	n.s.	104	10	3	209	Fisher's Exact Test
ATM_mono	0.836	n.s.	1	n.s.	93	12	14	209	Fisher's Exact Test
BIRC3_mono	0.066	trend	1	n.s.	100	1	7	209	Fisher's Exact Test
NOTCH1_mut	0.069	trend	1	n.s.	88	9	19	209	Fisher's Exact Test
SF3B1_mut	0.415	n.s.	1	n.s.	85	26	22	209	Fisher's Exact Test
X6q_delALL	0.595	n.s.	1	n.s.	98	6	9	209	Fisher's Exact Test
X13q_ALL	0.267	n.s.	1	n.s.	54	59	53	209	Fisher's Exact Test
X13del_homo	0.832	n.s.	1	n.s.	95	13	12	209	Fisher's Exact Test
X13q_het	0.330	n.s.	1	n.s.	66	46	41	209	Fisher's Exact Test
X13qdelRB1	0.743	n.s.	1	n.s.	84	24	23	209	Fisher's Exact Test
X13q_Ox	0.248	n.s.	1	n.s.	88	12	19	209	Fisher's Exact Test
X13q-Rossi	1	n.s.	1	n.s.	73	32	34	209	Fisher's Exact Test
Trisomy_12	0.002	**	0.100	trend	82	8	25	209	Fisher's Exact Test
Trisomy_18	0.060	trend	1	n.s.	102	0	5	209	Fisher's Exact Test
Trisomy_19	0.029	*	1	n.s.	101	0	6	209	Fisher's Exact Test
XPO1_ALL	0.160	n.s.	1	n.s.	100	13	7	209	Fisher's Exact Test
XPO1_gain	0.054	trend	1	n.s.	105	8	2	209	Fisher's Exact Test
XPO1_mutation	0.764	n.s.	1	n.s.	102	6	5	209	Fisher's Exact Test
SAMHD1_ALL	0.054	trend	1	n.s.	105	8	2	209	Fisher's Exact Test
SAMHD1_mut	0.006	**	0.254	n.s.	107	7	0	209	Fisher's Exact Test
pSAMHD1_cnLOH_Del	0.437	n.s.	1	n.s.	105	4	2	209	Fisher's Exact Test
MYD88_mut	1	n.s.	1	n.s.	105	1	2	209	Fisher's Exact Test
MED12mutation	0.360	n.s.	1	n.s.	106	3	1	209	Fisher's Exact Test
X8q_ALL	0.323	n.s.	1	n.s.	104	6	3	209	Fisher's Exact Test
X8q24_gain	0.203	n.s.	1	n.s.	106	4	1	209	Fisher's Exact Test
ZFPM2_mut	1	n.s.	1	n.s.	105	2	2	209	Fisher's Exact Test
Subclones	0.050	trend	1	n.s.					Wilcoxon Test
Total_num_CNAs	0.483	n.s.	1	n.s.					Wilcoxon Test
No_alteration	0.622	n.s.	1	n.s.	104	1	3	209	Fisher's Exact Test
Binet	0.770	n.s.	1	n.s.	72	36	35	209	Fisher's Exact Test
page_at_randomisation	0.100	trend	1	n.s.					Wilcoxon Test
patient_gender	0.443	n.s.	1	n.s.	33	76	74	209	Fisher's Exact Test
vh_mutation_status	0.0003	***	0.015	*	55	60	40	181	Fisher's Exact Test
ALC	0.017	*	0.671	n.s.					Wilcoxon Test
WBC	0.013	*	0.513	n.s.					Wilcoxon Test
cd38	0.707	n.s.	1	n.s.	45	40	59	147	Fisher's Exact Test

## Associations

Table 2: Uncorrected p-values for association between genetic lesions

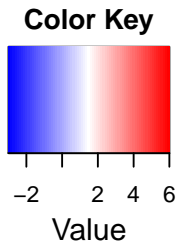
P	variables	TP53_ALL	TP53_del	TP53_cnLOH	TP53_mut	TP53_bi	ATM_ALL	ATM_mut	ATM_del	ATM_cnLOH	ATM_mtl	BIRC3_ALL	BIRC3_mut	BIRC3_del	ATM_bi	BIRC3_bi	X
P 1	TP53_ALL																
P 2	TP53_del		0	0.001	0	0	0.510	0.571	0.498	1	0.411	0.343	1	0.593	0.386	0.444	
P 3	TP53_cnLOH			1	0	0	0.274	0.530	0.429	1	1	0.422	1	0.642	0.634	1	
P 4	TP53_mut				0.005	0.002	1	0.632	0.505	1	1	1	1	1	1	1	
P 5	TP53_bi					0	0.173	0.186	0.275	1	0.631	0.087	0.642	0.189	0.181	1	
P 6	ATM_ALL						0.642	0.595	0.527	1	0.505	0.183	1	0.429	0.416	1	
P 7	ATM_mut							0	0	0.031	0.001	0	0.373	0	0	0.031	
P 8	ATM_del								0.003	0.011	0	0.111	0.197	0.017	0	0.647	
P 9	ATM_cnLOH									1	0.283	0	0.018	0	0	0.002	
P 10	ATM_mtl										1	1	1	1	0	1	
P 11	BIRC3_ALL											0.277	1	0.413	0.650	1	
P 12	BIRC3_mut												0	0	0	0.002	
P 13	BIRC3_del													0.042	1	0	
P 14	ATM_bi															0	
P 15	BIRC3_bi																1
P 16	X11q-mono																
P 17	ATM-mono																
P 18	BIRC3-mono																
P 19	NOTCH1_mut																
P 20	SF3B1_mut																
P 21	X6q--delALL																
P 22	X13q-ALL																
P 23	X13del.homo																
P 24	X13q.het																
P 25	X13qdelRBI																
P 26	X13q-Ox																
P 27	X13q-Rossi																
P 28	Trisomy_12																
P 29	Trisomy_18																
P 30	Trisomy_19																
P 31	XPO1-ALL																
P 32	XPO1-gain																
P 33	XPO1-mutation																
P 34	SAMHD1-ALL																
P 35	SAMHD1-mut																
P 36	SAMHD1.cnLOH.Del																
P 37	MYD88-mut																
P 38	MED12mutation																
P 39	X8q-ALL																
P 40	X8q24.gain																
P 41	ZFPM2-mut																
P 42	Subclones																
P 43	TotalNum.CNAs																
P 44	No.alteration																
P 45	Binet																
P 46	age.at.randomisation																
P 47	patient_gender																
P 48	vh_mutation-status																
P 49	MRD																
P 50	ALC																
P 51	WBC																
P 52	cd38																
P																	

Table 3: Corrected p-values for association between genetic lesions

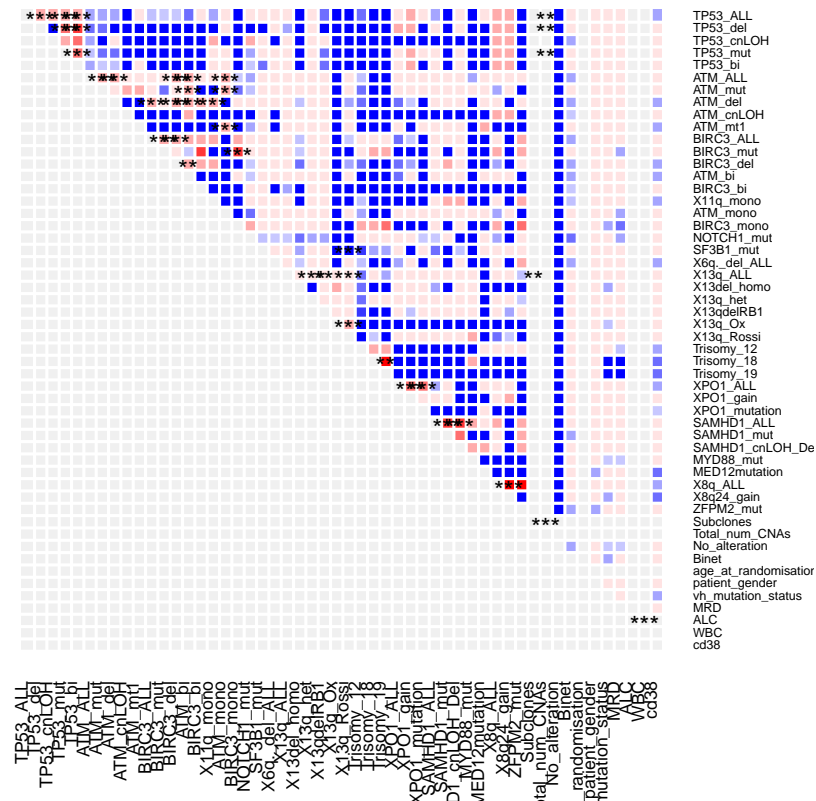
P	variables	TP53_ALL	TP53_del	TP53_cnLOH	TP53_mut	TP53_bi	ATM_ALL	ATM_mut	ATM_del	ATM_cnLOH	ATM_mnt1	BIRC3_ALL	BIRC3_mut	BIRC3_del	ATM_bi	BIRC3_bi	X
P 1	TP53_ALL			1	0	0	1	1	1	1	1	1	1	1	1	1	
P 2	TP53_del	0.001		1	0	0	1	1	1	1	1	1	1	1	1	1	
P 3	TP53_cnLOH			1	0	0	1	1	1	1	1	1	1	1	1	1	
P 4	TP53_mut				1	1	1	1	1	1	1	1	1	1	1	1	
P 5	TP53_bi					0	1	1	1	1	1	1	1	1	1	1	
P 6	ATM_ALL						1	1	1	1	1	0.014	1	1	1	1	
P 7	ATM_mut							0	0	1	1	1	1	0	0.001	1	
P 8	ATM_del								1	1	0.127	1	1	1	0	1	
P 9	ATM_cnLOH									1	1	0	1	0	0	1	
P 10	ATM_mnt1										1	1	1	1	0.368	1	
P 11	BIRC3_ALL											1	1	1	1	1	
P 12	BIRC3_mut											1	1	1	1	1	
P 13	BIRC3_del											0.014	1	0	1	1	
P 14	ATM_bi											1	1	1	1	1	
P 15	BIRC3_bi											1	1	1	0	1	
P 16	X11q-mono											1	1	1	1	1	
P 17	ATM-mono											1	1	1	1	1	
P 18	BIRC3-mono											1	1	1	1	1	
P 19	NOTCH1_mut											1	1	1	1	1	
P 20	SF3B1_mut											1	1	1	1	1	
P 21	X6q--delALL											1	1	1	1	1	
P 22	X13q-ALL											1	1	1	1	1	
P 23	X13del.homo											1	1	1	1	1	
P 24	X13q.het											1	1	1	1	1	
P 25	X13qdelRBI											1	1	1	1	1	
P 26	X13q-Ox											1	1	1	1	1	
P 27	X13q-Rossi											1	1	1	1	1	
P 28	Trisomy.12											1	1	1	1	1	
P 29	Trisomy.18											1	1	1	1	1	
P 30	Trisomy.19											1	1	1	1	1	
P 31	XPO1-ALL											1	1	1	1	1	
P 32	XPO1-gain											1	1	1	1	1	
P 33	XPO1-mutation											1	1	1	1	1	
P 34	SAMHD1-ALL											1	1	1	1	1	
P 35	SAMHD1_mut											1	1	1	1	1	
P 36	SAMHD1_cnLOH.Del											1	1	1	1	1	
P 37	MYD88_mut											1	1	1	1	1	
P 38	MED12mutation											1	1	1	1	1	
P 39	X8q-ALL											1	1	1	1	1	
P 40	X8q24.gain											1	1	1	1	1	
P 41	ZFPM2_mut											1	1	1	1	1	
P 42	Subclones											1	1	1	1	1	
P 43	Total_num.CNAs											1	1	1	1	1	
P 44	No.alteration											1	1	1	1	1	
P 45	Binet											1	1	1	1	1	
P 46	age.at.randomisation											1	1	1	1	1	
P 47	patient_gender											1	1	1	1	1	
P 48	vh_mutation-status											1	1	1	1	1	
P 49	MRD											1	1	1	1	1	
P 50	ALC											1	1	1	1	1	
P 51	WBC											1	1	1	1	1	
P 52	cd38											1	1	1	1	1	
P															0.003	0.024	0.590
																	1

Odds ratios and p-values for association between genes are represented in this heat map. Note that blue is mutually exclusive, red is associated. Also, the colour key is not symmetrical, colours used:

- -3 -> oddsratio<0.1
- -2 -> oddsratio>=0.1 oddsratio < 0.2
- -1 -> oddsratio>=0.2 oddsratio < 0.4
- 0 -> oddsratio>=0.4 oddsratio < 0.6
- 1 -> oddsratio>=0.6 oddsratio < 0.8
- 2 -> oddsratio>=1 oddsratio < 3
- 3 -> oddsratio>=3 oddsratio < 10
- 4 -> oddsratio>=10 oddsratio < 15
- 5 -> oddsratio>=15 oddsratio < 20
- 6 -> oddsratio>20



## Association for n=239



Model building - from here, only 209 data points will be used

## Association on model data

This was calculated to see if there are Colinearities that have to be taken into account for the modelling. There are fewer associations than in the 239 data set.

Table 4: Corrected p-values for association between genetic lesions, n=209

p	variables	TP53_ALL	TP53_del	TP53_cnLOH	TP53_mut	TP53_bi	ATM_ALL	ATM_mut	ATM_del	ATM_cnLOH	ATM_mt1	BIRC3_ALL	BIRC3_mut	BIRC3_bi	ATM_bi	BIRC3_bi	X11q
p 1	TP53_ALL			1	0	0	1	1	1	1	1	1	1	1	1	1	1
p 2	TP53_del		0.001	1	0	0	1	1	1	1	1	1	1	1	1	1	1
p 3	TP53_cnLOH			1	1	0	1	1	1	1	1	1	1	1	1	1	1
p 4	TP53_mut				1	0	1	1	1	1	1	1	1	1	1	1	1
p 5	TP53_bi					1	1	1	1	1	1	1	1	1	1	1	1
p 6	ATM_ALL						1	1	1	1	1	1	1	1	1	1	1
p 7	ATM_mut							0	0	1	1	0.014	1	1	0.001	1	0.57
p 8	ATM_del								1	1	0.127	1	1	1	0	1	1
p 9	ATM_cnLOH									1	1	0	1	1	0	1	0
p 10	ATM_mt1										1	1	1	1	0.368	1	1
p 11	BIRC3_ALL											1	1	1	1	1	1
p 12	BIRC3_mut												1	1	1	1	1
p 13	BIRC3_bi													1	1	1	1
p 14	ATM_bi														1	1	0.57
p 15	BIRC3_bi															1	1
p 16	X11q_mono																0
p 17	ATM_mono																1
p 18	BIRC3_mono																1
p 19	NOTCH1_mut																1
p 20	SF3B1_mut																1
p 21	X6q_del_ALL																1
p 22	X13q_ALL																1
p 23	X13del_homo																1
p 24	X13q_het																1
p 25	X13qdelRB1																1
p 26	X13q_Ox																1
p 27	X13q_Rossi																1
p 28	Trisomy_12																1
p 29	Trisomy_18																1
p 30	Trisomy_19																1
p 31	XPO1_ALL																1
p 32	XPO1_gain																1
p 33	XPO1_mutation																1
p 34	SAMHD1_ALL																1
p 35	SAMHD1_mut																1
p 36	SAMHD1_cnLOH_Del																1
p 37	MYD88_mut																1
p 38	MED12mutation																1
p 39	X8q_ALL																1
p 40	X8q24_gain																1
p 41	ZFPM2_mut																1
p 42	Subclones																1
p 43	TotalNum_CNAs																1
p 44	No.alteration																1
p 45	Binet																1
p 46	age_at_randomisation																1
p 47	patient_gender																1
p 48	vh_mutation_status																1
p 49	MRD																1
p 50	ALC																1
p 51	WBC																1
p 52	cd38																1



## 6

Table 5: Multiple log regression, n=209

	<i>Dependent variable:</i>					
	uncorrected all	uncorrected genetic	corrected all	corrected genetic	summarized genetic	summarized vhmud
Tri_ALL1					−0.83* (0.47)	−1.06** (0.54)
TP53_ALL1	1.11 (1.31)	1.49 (1.19)	1.49 (1.25)	1.04 (0.93)	2.71*** (0.77)	2.88*** (1.07)
TP53_del1	17.95 (9,579.62)	18.88 (5,618.88)				
TP53_cnLOH1	18.26 (6,522.64)	18.92 (5,344.79)				
TP53_mut1	17.39 (2,867.15)	17.51 (2,649.92)	16.16 (1,138.99)	16.93 (1,012.72)		
TP53_bi1	−18.12 (9,659.72)	−19.23 (4,622.34)				
ATM_ALL1	17.36 (3,180.05)	1.43 (1.65)	0.43 (0.47)	0.35 (0.43)	0.98*** (0.33)	0.83** (0.37)
ATM_mut1	−17.34 (3,180.05)	−1.38 (1.70)				
ATM_del1	−17.48 (3,180.05)	0.09 (1.47)	−0.29 (0.95)	0.52 (0.85)		
BIRC3_ALL1	−0.92 (1.44)	−1.50 (1.35)				
BIRC3_del1	1.09 (1.53)	1.37 (1.38)	0.57 (0.94)	0.52 (0.87)		
ATM_bi1	19.00 (3,180.05)	1.81 (1.21)	1.37* (0.72)	0.78 (0.64)		
X11q_mono1	1.56 (1.62)	0.15 (1.26)				
BIRC3_mono1						
NOTCH1_mut1	−0.91 (0.60)	−0.85 (0.58)			−0.58 (0.50)	−0.71 (0.55)
Trisomy_121	−0.60 (0.57)	−0.31 (0.50)	−1.04** (0.52)	−0.79* (0.45)		
Trisomy_181	−15.94 (2,665.11)	−16.06 (2,322.88)				
Trisomy_191	−15.53 (2,495.26)	−15.78 (2,197.33)				
XPO1_gain1	1.14 (1.00)	1.23 (0.98)				
SAMHD1_ALL1	−0.26 (1.65)	0.21 (1.33)			1.59* (0.83)	1.37 (0.85)
SAMHD1_mut1	18.72 (2,362.11)	18.51 (2,202.25)				
Subclones	−0.11 (0.29)	−0.07 (0.25)				
vh_mutation_statusunmutated	0.72* (0.40)		0.75** (0.35)			0.89** (0.36)
ALC	0.004 (0.01)					
WBC	−0.002 (0.01)					
SF3B1_mut1					−0.05 (0.37)	
Constant	−0.85** (0.39)	−0.44 (0.27)	−0.87*** (0.28)	−0.48** (0.21)	−0.44* (0.24)	−0.87*** (0.29)
Observations	178	209	181	209	209	181
Log Likelihood	−88.53	−108.17	−100.29	−120.56	−123.10	−101.52
Akaike Inf. Crit.	225.05	258.33	218.58	257.12	260.21	217.05

Note: \* p<0.1; \*\* p<0.05; \*\*\* p<0.01

## Missclassification Error

Table 6: Missclassification for summarized models

	model	true_MRD_neg	correct_MRD_neg	false_MRD_neg	true_MRD_pos	correct_MRD_pos	false_MRD_pos	missclasserror	unclassified
p1	sum_genetic	107	84	39	102	63	23	0.297	0
p2	sum_vhmud	95	68	30	86	56	27	0.315	29