

Circulating tumor DNA and bone marrow minimal residual disease negativity confers superior outcome for multiple myeloma patients

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Supplemental table 1: Information file

Excel table contains information on the progression-free and overall survival (PFS and OS) months, the best response based on the International Myeloma Working Group (IMWG) guidelines, the best minimal residual disease response (MRD) and fold change (FC) in the circulating tumour DNA (ctDNA) levels at cycle 3 day 1 (C3D1). F2A - if RespC3D1 = '1. CR+' and FC = 'NEG' then F2A='YES'; if RespC3D1 = '2. <CR' or FC = 'POS' then F2A='NO'; F2B - if MRD = 'NEG' and FC = 'NEG' then F2B='YES'; if MRD = 'POS' or FC = 'POS' then F2B='NO'; F2C - if RespC3D1 = '1. CR+' and MRD = 'NEG' and FC = 'NEG' then F2C='YES'; if RespC3D1 = '2. <CR' or MRD = 'POS' or FC = 'POS' then F2C='NO'.

Supplemental table 1														
Patient	Progression-Free Survival (PFS)	PFS_months	Overall Survival (OS)	OS_months	Best_IMWG	Best_MRD	C3D1_FC	FC_Num	RespC3D1	FC	MRD	F2A	F2B	F2C
ADE001	1	28.35318275	0	41.56057495	VGPR	Pos	-1	-1	2. <CR	NEG	POS	NO	NO	NO
ADE003	1	2.168377823	1	2.168377823	NA	NA	-.54	-0.54		NEG				
ADE004	0	38.73511294	0	38.73511294	sCR	NA	-.43	-0.43	1. CR+	NEG		YES		
ADE005	0	37.28952772	0	37.28952772	sCR	Neg	.61	0.61	1. CR+	POS	NEG	NO	NO	NO
ADE006	0	32.91991786	0	38.89938398	sCR	neg	-.74	-0.74	1. CR+	NEG	NEG	YES	YES	YES
ADE007	0	30.39014374	0	30.39014374	VGPR	neg	-.25	-0.25	2. <CR	NEG	NEG	NO	YES	NO
ALF002	1	12.15605749	1	21.12525667	CR	Pos	-.45	-0.45	1. CR+	NEG	POS	YES	NO	NO
ALF003	0	48.95277207	0	48.95277207	sCR	Neg	-.91	-0.91	1. CR+	NEG	NEG	YES	YES	YES
ALF004	1	8.837782341	0	48.06570842	VGPR	pos	-1	-1	2. <CR	NEG	POS	NO	NO	NO
ALF005	0	47.6386037	0	47.6386037	sCR	NA	.04	0.04	1. CR+	POS		NO	NO	NO
ALF006	1	13.30595483	1	20.43531828	PR	pos	-1	-1	2. <CR	NEG	POS	NO	NO	NO
ALF007	0	46.39014374	0	46.39014374	sCR	NA	-.27	-0.27	1. CR+	NEG		YES		
ALF008	1	3.54825462	0	45.37166324	NA	NA	-.76	-0.76		NEG				
ALF009	0	44.15605749	0	44.15605749	sCR	Neg	-.77	-0.77	1. CR+	NEG	NEG	YES	YES	YES
ALF010	1	23.72073922	0	44.32032854	sCR	pos	-.35	-0.35	1. CR+	NEG	POS	YES	NO	NO
ALF014	0	41.36344969	0	41.36344969	CR	neg	.44	0.44	1. CR+	POS	NEG	NO	NO	NO
ALF015	1	29.47022587	0	42.18480493	sCR	NA	-1	-1	1. CR+	NEG		YES		
ALF017	0	40.47638604	0	40.47638604	sCR	neg	-1	-1	1. CR+	NEG	NEG	YES	YES	YES
ALF018	1	41.52772074	0	41.19917864	PR	neg	-1	-1	2. <CR	NEG	NEG	NO	YES	NO
ALF019	0	43.63039014	0	43.63039014	NA	neg	1.01	1.01		POS	NEG	NO	NO	NO
ALF020	1	11.137577	1	11.137577	NA	NA	-.49	-0.49		NEG				
ALF021	0	36.1724846	0	36.1724846	sCR	neg	-.02	-0.02	1. CR+	NEG	NEG	YES	YES	YES
ALF022	0	42.34907598	0	42.34907598	NA	NA	-.69	-0.69		NEG				
ALF023	0	36.30390144	0	36.30390144	sCR	neg	-.14	-0.14	1. CR+	NEG	NEG	YES	YES	YES
ALF024	0	32.82135524	0	32.82135524	VGPR	neg	.14	0.14	2. <CR	POS	NEG	NO	NO	NO
ALF025	0	31.54004107	0	31.54004107	sCR	neg	-.18	-0.18	1. CR+	NEG	NEG	YES	YES	YES
ALF026	1	15.3100616	1	30.09445585	sCR	NA	-1	-1	1. CR+	NEG		YES		
ALF027	0	28.97741273	0	28.97741273	VGPR	neg	-1	-1	2. <CR	NEG	NEG	NO	YES	NO
ALF028	1	3.252566735	1	19.1211499	NA	NA	.18	0.18		POS		NO	NO	NO
CAN001	1	0.361396304	1	4.533880903	NA	NA	-.39	-0.39		NEG				
RNS001	0	40.08213552	0	40.08213552	sCR	NA	-.18	-0.18	1. CR+	NEG		YES		
RNS002	0	36.66529774	0	36.66529774	sCR	neg	.56	0.56	1. CR+	POS	NEG	NO	NO	NO
SVM001	0	42.67761807	0	42.67761807	sCR	NA	-.59	-0.59	1. CR+	NEG		YES		
SVM002	0	47.57289528	0	47.57289528	sCR	Neg	-1	-1	1. CR+	NEG	NEG	YES	YES	YES
SVM003	0	38.63655031	0	38.63655031	VGPR	neg	-.68	-0.68	2. <CR	NEG	NEG	NO	YES	NO
SVM004	0	37.97946612	0	37.97946612	sCR	neg	-1	-1	1. CR+	NEG	NEG	YES	YES	YES
SVM005	0	36.99383984	0	36.99383984	sCR	neg	-1	-1	1. CR+	NEG	NEG	YES	YES	YES
SVM006	0	38.01232033	0	38.01232033	VGPR	Neg	-.8	-0.8	2. <CR	NEG	NEG	NO	YES	NO
SVM007	1	14.48870637	0	33.44558522	VGPR	pos	-1	-1	2. <CR	NEG	POS	NO	NO	NO
SVM008	1	23.91786448	0	32.88706366	VGPR	pos	-.52	-0.52	2. <CR	NEG	POS	NO	NO	NO
SVM009	0	31.14579055	0	31.14579055	PR	pos	-.91	-0.91	2. <CR	NEG	POS	NO	NO	NO

Supplemental table 2: Variant allele frequency (VAF) of circulating tumour DNA mutations at baseline and cycle 3 D1 (C3D1). A list of mutations identified at baseline (x) in each of the patients analysed is shown with relevant changes in specific mutations (y) at C3D1. The fold change (FC) is calculated as $(y-x)/x$. A negative value is deemed as a decrease and a positive value is deemed as an increase. An average FC is calculated for each patient.

Supplemental table 2				
				Fold difference VAF
ALF002	Mutation	Baseline	C3D1	B vs C3D1
	BRAF	5.09	0.00	-1.00
	KRAS	4.51	0.00	-1.00
	KRAS	3.56	0.00	-1.00
	GNAS	0.62	0.00	-1.00
	ATM	2.15	3.75	0.74
	CCND1	0.71	0.75	0.06
	CYLD	0.49	0.52	0.06
				-0.45
ALF003	Mutation	Baseline	C3D1	B vs C3D1
	GNAS	2.24	0.83	-0.63
	ATR	2.22	0	-1.00
	GNAS	1.5	0	-1.00
	TRAF3	0.83	0	-1.00
				-0.91
ALF005	Mutation	Baseline	C3D1	B vs C3D1
	EGR1	0.51	0.53	0.04
				0.04
ALF008	Mutation	Baseline	C3D1	B vs C3D1
	RB1	0.59	0.25	-0.58
	EGR1	2.48	1.34	-0.46
	ATM	2.07	0	-1.00
	ACTG1	2.17	0	-1.00
				-0.76
ALF009	Mutation	Baseline	C3D1	B vs C3D1
	KRAS	4.93	0	-1.00
	PIK3CA	1.7	0	-1.00
	FGFR3	1.46	0	-1.00
	ATM	0.69	0.63	-0.09
				-0.77
ALF010	Mutation	Baseline	C3D1	B vs C3D1

	EGR1	0.99	0.98	-0.01
	NRAS	0.68	0	-1.00
	ATR	0.67	0	-1.00
	ATR	0.56	0.56	0.00
	TRAF3	0.32	0.62	0.94
	BRAF	2.97	0	-1.00
				-0.35
ALF011	Mutation	Baseline	C3D1	
	None detected			
ALF012	Mutation	Baseline	C3D1	
	None detected			
ALF014	Mutation	Baseline	C3D1	B vs C3D1
	ATM	0.84	0.58	-0.31
	ATR	1.31	0	-1.00
				0.44
ALF016	Mutation	Baseline	C3D1	
	ATR	2.07	Relapse occurred	
	RB1	0.58		
ALF020	Mutation	Baseline	C3D1	B vs C3D1
	PRDM1	0.67	0	-1.00
	ATR	1.17	0.9	-0.23
	ATM	0.42	0.54	0.29
	ATR	1.27	0	-1.00
				-0.49
ADE-001	Mutation	Baseline	C3D1	B vs C3D1

	ATR	1.33	0	-1.00
				-1.00
ADE-004	Mutation	Baseline	C3D1	B vs C3D1
	DIS3	1.61	0	-1.00
	IRF4	1.12	0	-1.00
	NRAS	0.89	0	-1.00
	IRF4	0.56	0.67	0.20
	RB1	0.51	0.48	-0.06
	PRDM1	0.39	0.51	0.31
				-0.43
ADE-005	Mutation	Baseline	C3D1	B vs C3D1
	ATM	0.89	1.39	0.56
	FGFR3	0.65	1.08	0.66
				0.61
SVM-002	Mutation	Baseline	C3D1	B vs C3D1
	PIK3CA	1.1	0	-1.00
				-1.00
SVM-006	Mutation	Baseline	C3D1	B vs C3D1
	RB1	1.12	0.68	-0.39
	ACTG1	1.16	0	-1.00
	PIK3CA	2.04	0	-1.00
				-0.80
ALF-004	Mutation	Baseline	C3D1	B vs C3D1
	CYLD	0.7	0	-1.00
				-1.00
ALF-006	Mutation	Baseline	C3D1	B vs C3D1
	ATR	1.01	0	-1.00

	DIS3	2.03	0	-1.00
				-1.00
ALF-007	Mutation	Baseline	C3D1	B vs C3D1
	ATM	0.99	1.44	0.45
	ATR	1.86	0	-1.00
				-0.27
ALF-015	Mutation	Baseline	C3D1	B vs C3D1
	TP53	2.7	0	-1.00
ALF-017	Mutation	Baseline	C3D1	B vs C3D1
	FGFR3	1	0	-1.00
				-1.00
ALF-018	Mutation	Baseline	C3D1	B vs C3D1
	FGFR3	0.91	0	-1.00
	ATR	2.18	0	-1.00
				-1.00
ALF-019	Mutation	Baseline	C3D1	B vs C3D1
	ATM	0.8	0	-1.00
	DIS3	0.68	1.18	0.74
	FGFR3	0.64	0.98	0.53
	NRAS	0.45	1.48	2.29
	NRAS	0.44	1.47	2.34
	ATR	0.31	0.68	1.19
				1.01
ALF-021	Mutation	Baseline	C3D1	B vs C3D1

	CYLD	0.55	0	-1.00
	EGR1	0.23	0.45	0.96
				-0.02
ALF-022	Mutation	Baseline	C3D1	B vs C3D1
	CYLD	1.93	0	-1
	ATM	1.07	0	-1
	EGR1	0.63	0.39	-0.380952381
	ATR	0.61	0.37	-0.393442623
				-0.69
ALF-023	Mutation	Baseline	C3D1	B vs C3D1
	ATM	0.58	0.5	-0.14
				-0.14
ALF-024	Mutation	Baseline	C3D1	B vs C3D1
	RB1	0.35	0.4	0.14
				0.14
ALF-025	Mutation	Baseline	C3D1	B vs C3D1
	EGR1	2.42	3.58	0.48
	EGR1	2.18	2.13	-0.02
	FGFR3	1.62	0	-1.00
				-0.18
ALF-026	Mutation	Baseline	C3D1	B vs C3D1
	RB1	0.72	0	-1.00
				-1.00
ALF-027	Mutation	Baseline	C3D1	B vs C3D1

	ATR	1.38	0	-1.00
				-1.00
ALF-028	Mutation	Baseline	C3D1	B vs C3D1
	FGFR3	1.25	0	-1.00
	RB1	0.31	0.7	1.26
	FGFR3	0.25	0.32	0.28
				0.18
SVM-001	Mutation	Baseline	C3D1	B vs C3D1
	ACTG1	1.4	0	-1.00
	FGFR3	1.14	0	-1.00
	RB1	0.46	0.56	0.22
				-0.59
SVM-003	Mutation	Baseline	C3D1	B vs C3D1
	FGFR3	1.17	0	-1.00
	FGFR3	1.06	0	-1.00
	ATR	0.58	0.34	-0.41
	FGFR3	0.5	0.35	-0.30
				-0.68
SVM-004	Mutation	Baseline	C3D1	B vs C3D1
	FGFR3	3.75	0	-1.00
				-1.00
SVM-005	Mutation	Baseline	C3D1	B vs C3D1
	DIS3	2.08	0	-1.00
				-1.00

SVM-007	Mutation	Baseline	C3D1	B vs C3D1
	PIK3CA	1.97	0	-1.00
	FGFR3	1.28	0	-1.00
				-1.00
SVM-008	Mutation	Baseline	C3D1	B vs C3D1
	EGR1	3.04	1.45	-0.52
SVM-009	Mutation	Baseline	C3D1	B vs C3D1
	EGR1	3.93	1.07	-0.73
	DIS3	2.32	0	-1.00
	FGFR3	1.14	0	-1.00
				-0.91
CAN-001	Mutation	Baseline	C3D1	B vs C3D1
	DIS3	27.8	15.52	-0.44
	NRAS	13.08	6.67	-0.49
	NRAS	1.97	2.43	0.23
	FGFR3	1.67	0	-1.00
	ATM	1.21	0	-1.00
	ATM	1.21	0	-1.00
	ATR	0.27	0.53	0.96
				-0.39
ADE-002	Mutation	Baseline	C3D1	
	None detected			
ADE-003	Mutation	Baseline	C3D1	B vs C3D1

	TP53	1.48	0	-1.00
	DIS3	1.4	1.57	0.12
	EGR1	0.83	0	-1.00
	ATR	0.5	0.36	-0.28
				-0.54
ADE-006	Mutation	Baseline	C3D1	B vs C3D1
	EGR1	3.72	1.96	-0.47
	CYLD	1.03	0	-1.00
				-0.74
ADE-007	Mutation	Baseline	C3D1	B vs C3D1
	ATR	1.71	0.59	-0.65
	RB1	0.4	0.46	0.15
				-0.25
RNS-001	Mutation	Baseline	C3D1	B vs C3D1
	DIS3	6.03	1.77	-0.71
	EGR1	1.66	0.95	-0.43
	ATM	0.52	0.83	0.60
				-0.18
RNS-002	Mutation	Baseline	C3D1	B vs C3D1
	ATM	0.62	0.97	0.56
				0.56
RNS-003	Mutation	Baseline	C3D1	
	BRAF	2.32	not available	
	BRAF	2.87		

RNS-004	Mutation	Baseline	C3D1	
		1.67	not available	
RNS-005	Mutation	Baseline	C3D1	
		failed sequencing		