LETTER TO THE EDITOR

Clinical and genomic features of macrofocal multiple myeloma: a distinct profile

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Supplemental Materials

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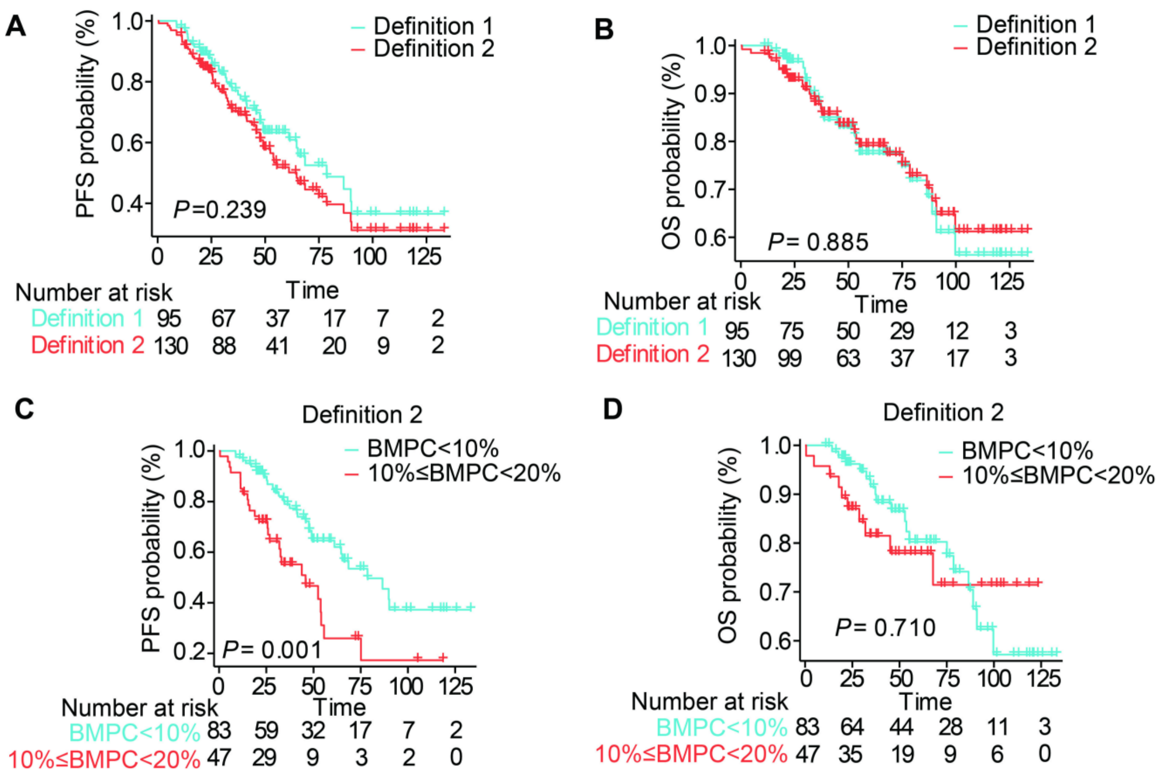
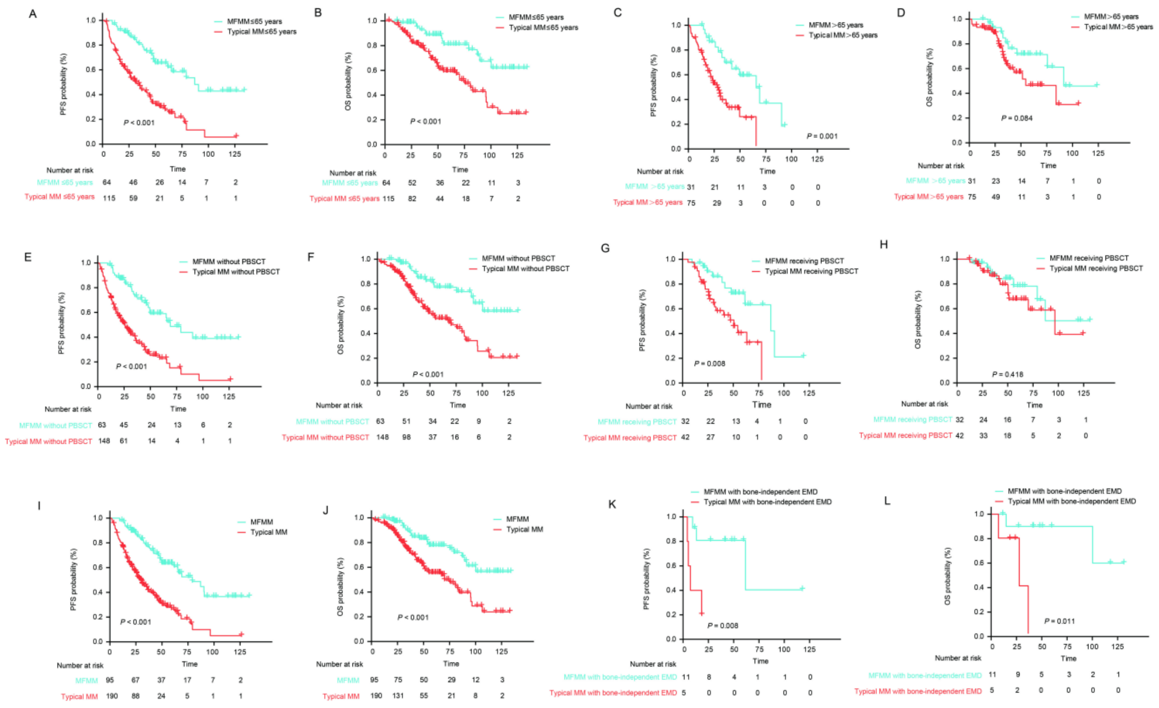


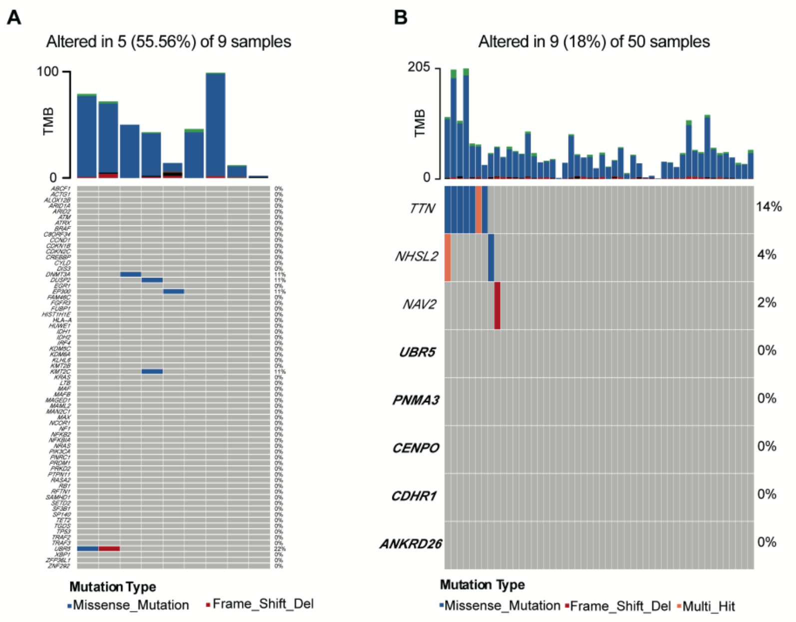
Supplemental figure 1. Survival outcomes in atypical MM. **A,** PFS in atypical MM meeting Definition 1 vs 2. **B,** OS in atypical MM meeting Definition 1 vs 2. **C,** PFS in atypical MM meeting Definition 2 with BMPCs <10% vs BMPCs ⩾10% but <20%. **D,** OS in atypical MM meeting Definition 2 with BMPCs <10% vs BMPCs ⩾10% but <20%.

Abbreviations: BMPCs: Bone marrow plasma cells; OS: Overall survival; PFS: Progression-free survival.



Supplemental figure 2. Survival outcomes in patients with MFMM or typical MM in different groups. A, PFS in MFMM vs typical MM with aged ≤65 years. **B,** OS in MFMM vs typical MM with aged ≤65 years. **C,** PFS in MFMM vs typical MM with aged >65 years. **D,** OS in MFMM vs typical MM with aged >65 years. **E,** PFS in MFMM vs typical MM without PBSCT. **F,** OS in MFMM vs typical MM without PBSCT. **G,** PFS in MFMM vs typical MM receiving PBSCT. **H,** OS in MFMM vs typical MM receiving PBSCT. **I,** PFS in MFMM vs typical MM. **J,** OS in MFMM vs typical MM. **K,** PFS in typical MM vs MFMM with bone-independent EMD. **L,** OS in typical MM vs MFMM with bone-independent EMD.

Abbreviations: EMD: extramedullary multiple myeloma; MFMM: macrofocal multiple myeloma; MM: multiple myeloma; OS: overall survival; PFS: progression-free survival; PBSCT: Peripheral blood stem cell transplantation.



Supplemental figure 3. Waterfall of 67 MM driver genes in MFMM and 8 highly mutational genes in typical MM. A, Waterfall of 67 MM driver genes in MFMM (n =9). **B,** Waterfall of 8 highly mutated genes in typical MM (n =50). Among the 8 high-frequency genes in MFMM, 3 genes are also observed in typical MM, and he remaining 5 genes, including ANKRD26, CDHR1, PNMA3, CENPO and UBR5 are uniquely present in MFMM.

Abbreviations: MFMM, macrofocal multiple myeloma; MM, multiple myeloma.

Supplemental table 1. Baseline information and 5 exclusive genes of MFMM patients in WES cohort

Clinical information									FISH						
Patient ID	M-protein type	Heavy chain	Light chain	Gender	Age at diagnosis	DS stage	ISS stage	R-ISS stage	IGH translocation	t(4;14)	t(11;14)	t(14;16)	17p-	13q-	1q21+
NDMM 01	κ	ND	κ	Male	45	ⅢA	Ⅰ	Ⅰ	14	0	0	0	6	11	16
NDMM 02	IgG-κ	IgG	κ	Male	62	ⅢA	Ⅰ	Ⅰ	0	0	0	0	0	0	0
NDMM 03	IgG-κ	IgG	κ	Male	52	ⅢA	Ⅰ	Ⅰ	34	0	0	0	12	6	80
NDMM 04	IgG-λ	IgG	λ	Male	70	ⅢA	Ⅰ	Ⅱ	62	60	0	0	9	10	86
NDMM 05	IgG-κ	IgG	κ	Male	64	ⅢA	Ⅰ	Ⅰ	26	0	0	0	3	2	40
NDMM 06	κ	ND	κ	Male	58	ⅠA	Ⅰ	Ⅰ	32	0	0	0	12	3	29
NDMM 07	IgG-κ	IgG	κ	Female	55	ⅢA	Ⅰ	Ⅱ	50	46	0	0	22	6	17
NDMM 08	IgG-λ	IgG	λ	Male	74	ⅢA	Ⅰ	Ⅰ	90	0	94	0	2	1	10
RRMM 01	IgD-λ	IgD	λ	Male	64	ⅢA	Ⅱ	Ⅱ	15	0	0	0	10	3	60

5 genes specific in MFMM																		
Chromosome	Start_Position	End_Position	Reference_Allele	Tumor_Seq	Tumor_Sample	Hugo_Symbol	Variant_Classification	tx	exon	txChange	aaChange	Variant_Type	sample_id	Func.refGene	Gene.refGene	GeneDetail.refGene	ExonicFunc.refGene	AAChange.refGene

				_Allele2	_Barcode													
chr10	27035701	27035701	A	T	RA201908290198	ANKRD26	Missense_Mutation	NM_001256053	exon24	c.T2746A	p.L916M	SNP	15_sample	exonic	ANKRD26	.	nonsynonymous SNV	ANKRD26:NM_001256053:exon24:c.T2746A:p.L916M,ANKRD26:NM_014915:exon24:c.T2749A:p.L917M
chr10	27035187	27035187	C	T	RA201910120076	ANKRD26	Missense_Mutation	NM_001256053	exon24	c.G3260A	p.R1087K	SNP	15_sample	exonic	ANKRD26	.	nonsynonymous SNV	ANKRD26:NM_001256053:exon24:c.G3260A:p.R1087K,ANKRD26:NM_014915:exon24:c.G3263A:p.R1088K
chr10	84219208	84219208	G	A	RA201910120076	CDHR1	Missense_Mutation	NM_001171971	exon17	c.G2170A	p.A724T	SNP	15_sample	exonic	CDHR1	.	nonsynonymous SNV	CDHR1:NM_001171971:exon17:c.G2170A:p.A724T
chr10	84211081	84211081	C	A	RA202007130147	CDHR1	Missense_Mutation	NM_001171971	exon13	c.C1401A	p.D467E	SNP	15_sample	exonic	CDHR1	.	nonsynonymous SNV	CDHR1:NM_001171971:exon13:c.C1401A:p.D467E,CDHR1:NM_033100:exon13:c.C1401A:p.D467E
chrX	153057493	153057493	-	GTCCAGAACTCT	RA202009110167	PNMA3	In_Frame_Ins	NM_001282535	exon2	c.438_439insGTCCAGAACTCT	p.Q146_T147insVQNSGDIV	INS	15_sample	exonic	PNMA3	.	nonframeshift insertion	PNMA3:NM_001282535:exon2:c.438_439insGTCCA

				GGTGATATAGTC						GGTGATATAGTC								GAACTCTGGTGATATAGTC:p.Q146_T147insVQNSGDIV,PNMA3:NM_013364:exon2:c.438_439insGTCCAGAACTCTGGTGATATAGTC:p.Q146_T147insVQNSGDIV
chrX	153057493	153057493	-	GTCCAGA	RA202108030178	PNMA3	Frame_Shift_Ins	NM_001282535	exon2	c.438_439insGTCCAGA	p.T147Vfs*37	INS	15_sample	exonic	PNMA3	.	frameshift insertion	PNMA3:NM_001282535:exon2:c.438_439insGTCCAGA:p.T147Vfs*37,PNMA3:NM_013364:exon2:c.438_439insGTCCAGA:p.T147Vfs*37
chr8	102361199	102361199	G	C	RA201908290198	UBR5	Missense_Mutation	NM_001282873	exon3	c.C115G	p.P39A	SNP	15_sample	exonic	UBR5	.	nonsynonymous SNV	UBR5:NM_001282873:exon3:c.C115G:p.P39A,UBR5:NM_015902:exon3:c.C115G:p.P39A
chr8	102305098	102305098	A	-	RA202007130147	UBR5	Frame_Shift_Del	NM_001282873	exon21	c.2814delT	p.E940Kfs*47	SNP	15_sample	exonic	UBR5	.	frameshift deletion	UBR5:NM_001282873:exon21:c.28

																		14delT:p.E940Kfs*47,UBR5:NM_015902:exon21:c.2814delT:p.E940Kfs*47
chr2	24815499	24815499	C	A	RA202004140134	CENPO	Missense_Mutation	NM_001199803	exon4	c.C319A	p.L107I	SNP	15_sample	exonic	CENPO	.	nonsynonymous SNV	CENPO:NM_001199803:exon4:c.C319A:p.L107I,CENPO:NM_001322101:exon5:c.C337A:p.L113I,CENPO:NM_024322:exon5:c.C337A:p.L113I
chr2	24799803	24799803	C	T	RA202010120124	CENPO	Nonsense_Mutation	NM_001199803	exon2	c.C157T	p.R53X	SNP	15_sample	exonic	CENPO	.	stopgain	CENPO:NM_001199803:exon2:c.C157T:p.R53X,CENPO:NM_001322101:exon3:c.C175T:p.R59X,CENPO:NM_024322:exon3:c.C175T:p.R59X

Abbreviations: NDMM: new diagnosed multiple myeloma; RRMM: relapsed/refractory multiple myeloma; M-protein: monoclonal protein; IgG: immunoglobulin G; IgD: immunoglobulin D; ND: not detected; DS: Durie-Salmon; ISS: international Staging System; R-ISS: revised international staging system; FISH: fluorescence in situ hybridization; IGH: immunoglobulin heavy chain gene locus.