

Supplementary Table 1 | Detailed information about first-line therapeutic regimens of patients with MM-alone, MM-AL and pAL-alone.

First-line therapeutic regimens, n (%)			MM-alone, n=658	MM-AL, n=106	pAL-alone, n=151
PI-based	Bortezomib	BCd	244 (37.1)	53 (50.0)	92 (60.9)
		Bd	79 (12.0)	23 (21.7)	14 (9.3)
		BAd	5 (0.7)	/	/
		B	3 (0.5)	/	1 (0.7)
	Ixazomib	Id	26 (4.0)	15 (14.2)	19 (12.6)
		ICd	5 (0.7)	2 (1.9)	1 (0.7)
		IAd	1 (0.2)	/	/
		I	1 (0.2)	/	/
IMiD-based	Thalidomide	CTd	11 (1.7)	/	/
		Td	7 (1.1)	/	/
	Lenalidomide	Rd	11 (1.7)	/	/
		R	2 (0.3)	/	/
		RCd	1 (0.2)	/	2 (1.3)
		RMD	/	/	1 (0.7)
PI+IMiD-based	BRd		121 (18.4)	6 (5.7)	7 (4.6)
	BTd		94 (14.3)	3 (2.8)	2 (1.3)
	IRd		35 (5.3)		
	BATd		5 (0.7)	/	/
	BPd		5 (0.7)	/	/
	BCTd		1 (0.2)	/	/
Dara-based	Dara-Bd		/	3 (2.8)	1 (0.7)
	Dara-BRd		1 (0.2)	/	/
	Dara-BCd		/	/	8 (5.3)
	Dara-d		/	/	1 (0.7)
Chemo-only		others	/	1 ^a (0.9)	2 ^b (1.3)

Abbreviations: PI, proteasome inhibitor; B, Bortezomib; C, Cyclophosphamide; d, Dexamethasone; A, Adriamycin; I, Ixazomib; IMiD, immunomodulatory drug; T, Thalidomide; R, Lenalidomide; M, Melphalan; P, Pomalidomide; Dara, Daratumumab;

^a including one patient treated with CP (cyclophosphamide+ prednisone)

^b including patients treated with Dexamethasone and supportive therapy, respectively

Supplementary Table 2 | Comparison of treatment response and MRD status after first-line CyBorD in MM-alone, MM-AL and pAL-alone groups

	MM-alone N=658	MM-AL N=106	pAL-alone N=151	P value (MM-alone vs. MM-AL)	P value (MM-AL vs. pAL-alone)	P value (overall)
CyBorD^a						
Hematologic response based on IMWG consensus criteria, n/N (%)						
CR	90/218 (41.3)	9/35 (25.7)	-	0.080		
≥VGPR	148/218 (67.9)	16/35 (45.7)	-	0.011		
ORR	194/218 (89.0)	24/35 (68.6)	-	0.001		
Hematologic response based on AL consensus criteria, n/N (%)						
CR	-	9/35 (25.7)	32/74 (43.2)		0.078	
≥VGPR	-	22/35 62.9)	58/74 (78.4)		0.087	
ORR	-	27/35 (77.1)	63/74 (85.1)		0.304	
Organ response, n/N (%)						
Cardiac	-	18/47 (38.3)	28/79 (35.4)		0.748	
Renal	-	9/19 (47.4)	14/36 (38.9)		0.544	
Hepatic	-	0/5 (0)	3/8 (37.5)		0.118	
MRD negative, n/N (%)	74/232 (31.9)	5/23 (21.7)	25/55 (45.5)	0.315	0.050	0.074

CyBorD, Cyclophosphamide + Bortezomib + Dexamethasone.

^a Patients receiving CyBorD: MM-alone, n=244 (37.1%), MM-AL, n=53 (50.0%), pAL-alone, n=92 (60.9%)

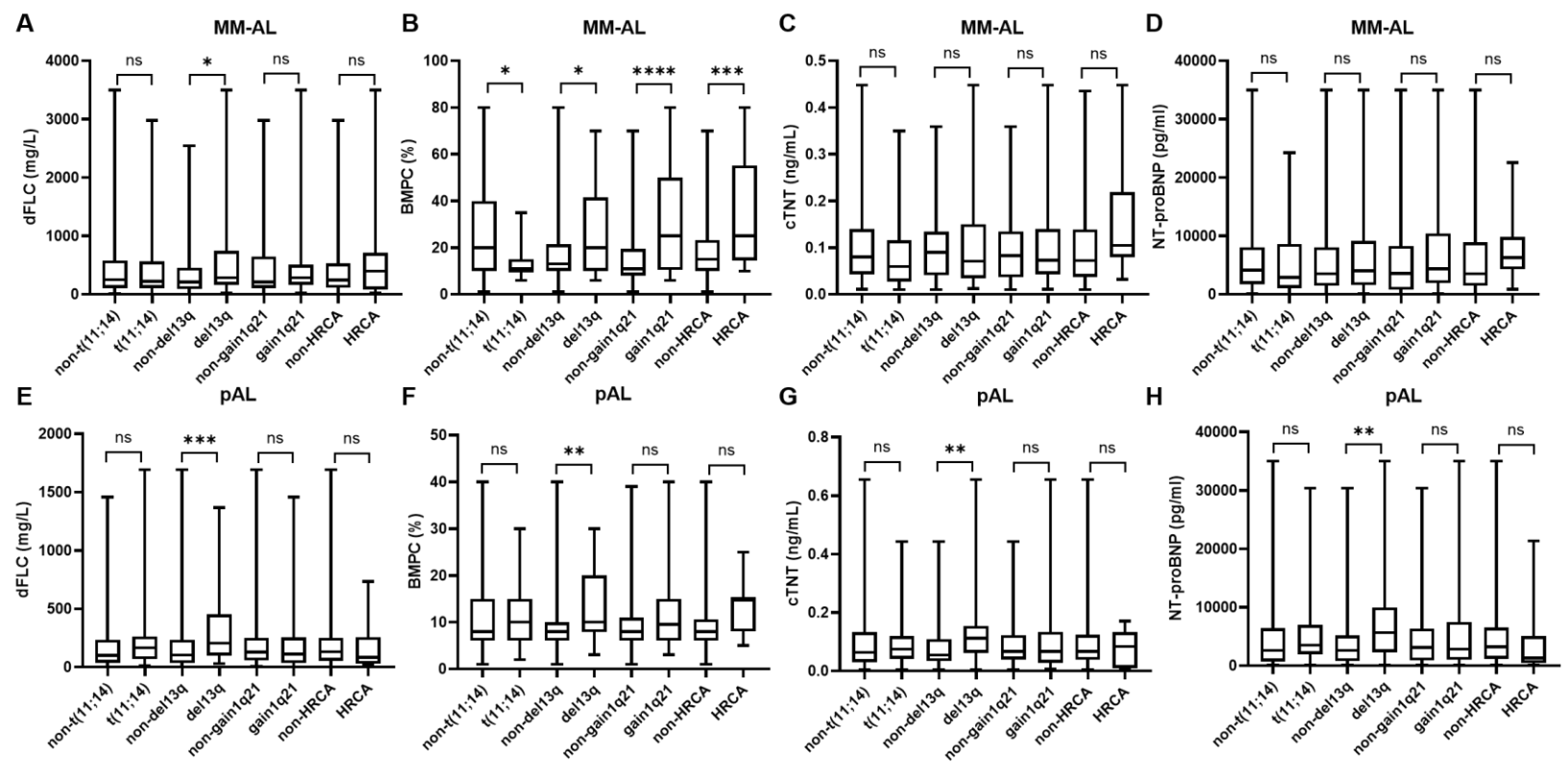
Supplementary Table 3 | Rate of ≥VGPR of patients with different plasma cell dyscrasias by FISH status by regimen type

	MM-alone	P value	MM-AL	P value	pAL-alone	P value
All regimens	N=658		N=106		N=151	
normal	104/143 (72.7%)	0.259	8/18 (44.4%)	0.160	28/32 (87.5%)	0.028
abnormal	289/427 (67.7%)		36/57 (63.2%)		55/82 (67.1%)	
HRCA-negative	283/405 (69.9%)	0.453	37/63 (58.7%)	0.980	75/104 (72.1%)	0.592
HRCA-positive	110/165 (66.7%)		7/12 (58.3%)		8/10 (80.0%)	
t(11;14)-negative	307/421 (72.9%)	<0.001	36/57 (63.2%)	0.247	51/63 (81.0%)	0.043
t(11;14)-positive	44/85 (51.8%)		7/15 (46.7%)		32/50 (64.0%)	
del13q14-negative	191/291 (65.6%)	0.059	23/44 (52.3%)	0.127	64/88 (72.7%)	0.972
del13q14-positive	195/267 (73.0%)		21/30 (70.0%)		19/26 (73.1%)	
gain1q21-negative	189/266 (71.1%)	0.310	21/39 (53.8%)	0.299	62/84 (73.8%)	0.687
gain1q21-positive	204/304 (67.1%)		23/35 (65.7%)		21/30 (70.0%)	
Bortezomib-based	N=560		N=79		N=118	
normal	98/128 (76.6%)	0.097	5/12 (41.7%)	0.057	23/25 (92.0%)	0.063
abnormal	254/369 (68.8%)		30/42 (71.4%)		49/66 (74.2%)	
HRCA-negative	249/349 (71.3%)	0.694	29/44 (65.9%)	0.724	65/82 (79.3%)	0.917
HRCA-positive	103/148 (69.6%)		6/10 (60.0%)		7/9 (77.8%)	
t(11;14)-negative	274/368 (74.5%)	<0.001	27/39 (69.2%)	0.484	42/50 (84.0%)	0.289
t(11;14)-positive	37/69 (53.6%)		7/12 (58.3%)		30/40 (75.0%)	
del13q14-negative	172/259 (66.4%)	0.022	20/33 (60.6%)	0.283	56/72 (77.8%)	0.539
del13q14-positive	173/228 (75.9%)		15/20 (75.0%)		16/19 (84.2%)	
gain1q21-negative	173/235 (73.6%)	0.195	18/29 (62.1%)	0.502	54/68 (79.4%)	0.907
gain1q21-positive	179/262 (68.3%)		17/24 (70.8%)		18/23 (78.3%)	

Supplementary Table 4 | Demographics and clinical characteristics of patients with MM-AL receiving or not receiving maintenance therapy

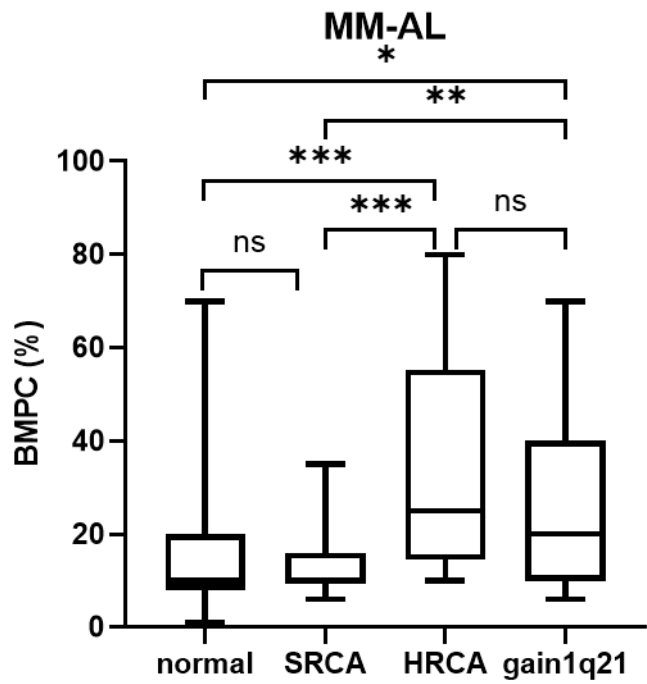
	With maintenance N=17	Without maintenance N=15	P value
Male, n(%)	11 (64.7)	11 (73.3)	0.599
Age (years), median(range)	61 (51-81)	66 (52-78)	0.478
ECOG performance status, n(%)			
0-2	14 (82.4)	14 (93.3)	0.349
>2	3 (17.6)	1 (6.7)	
Organ involvement, n(%)			
Heart	14 (82.4)	12 (80.0)	0.865
Kidney	4 (23.5)	6 (40.0)	0.316
Liver	1 (5.9)	1 (6.7)	0.927
Number of involved organs, median (range)	2 (1-3)	2 (1-4)	0.682
Lambda restriction, n(%)	10 (58.8)	10 (66.7)	0.647
dFLC (mg/L), median(range)	282.7 (25.1-3500.3)	177.6 (13.4-2580.2)	0.370
NT-proBNP(pg/mL), median(range)	1518 (124.4-33997)	1161 (61-35000)	0.710
cTNT(ng/mL), median(range)	0.043 (0.011-0.405)	0.0395 (0.01-0.175)	0.551
Serum alkaline phosphatase(U/L), median(range)	78 (57-285)	82 (45-700)	0.799
Serum creatine(μmol/L), median(range)	89 (47-272)	95 (51-272)	0.799
eGFR(mL/min/1.73m ²), median(range)	69 (21-108)	71.5 (22-96)	0.997
BMPCs(%),median(range)	20 (10-70)	10 (7-70)	0.030
European 2015 modification of 2004 Mayo model, I / II /IIIa/IIIb (%)	23.5/ 11.8/ 52.9/ 11.8	13.3/ 26.7/ 40.0/ 20.0	0.569
Revised 2012 Mayo model, I / II /III/IV (%)	11.8/ 23.5/ 29.4/ 35.3	6.7/ 26.7/ 40.0/ 26.7	0.873
First-line induction therapy, n(%)			
PI-based	14 (82.4)	13 (86.7)	0.737
PI+IMiD-based	3 (17.6)	2 (13.3)	0.737
Cycles of induction therapy, median (range)	9 (4-12)	5.5 (2-9)	<0.001
Pre-maintenance hematologic response (AL criteria), n(%)			
CR	5 (29.4)	5 (33.3)	0.811
≥VGPR	16 (94.1)	13 (86.7)	0.471
≥PR	17 (100)	15 (100)	/
Pre-maintenance organ response, n(%)			
Heart	14/17 (82.4)	11/12 (91.7)	0.474
Kidney	4/4 (100)	4/6 (66.7)	0.197
Liver	0/1 (0)	0/1 (0)	/

Supplementary Figure 1 | Association of high risk features with cytogenetic abnormalities (CAs) in patients with AL amyloidosis. Association of levels of dFLC (A), BMPC (B), cTNT (C) and NT-proBNP (D) with CAs in patients with MM-AL. Associations of levels of dFLC (E), BMPC (F), cTNT (G) and NT-proBNP (H) with CAs in patients with pAL-alone.



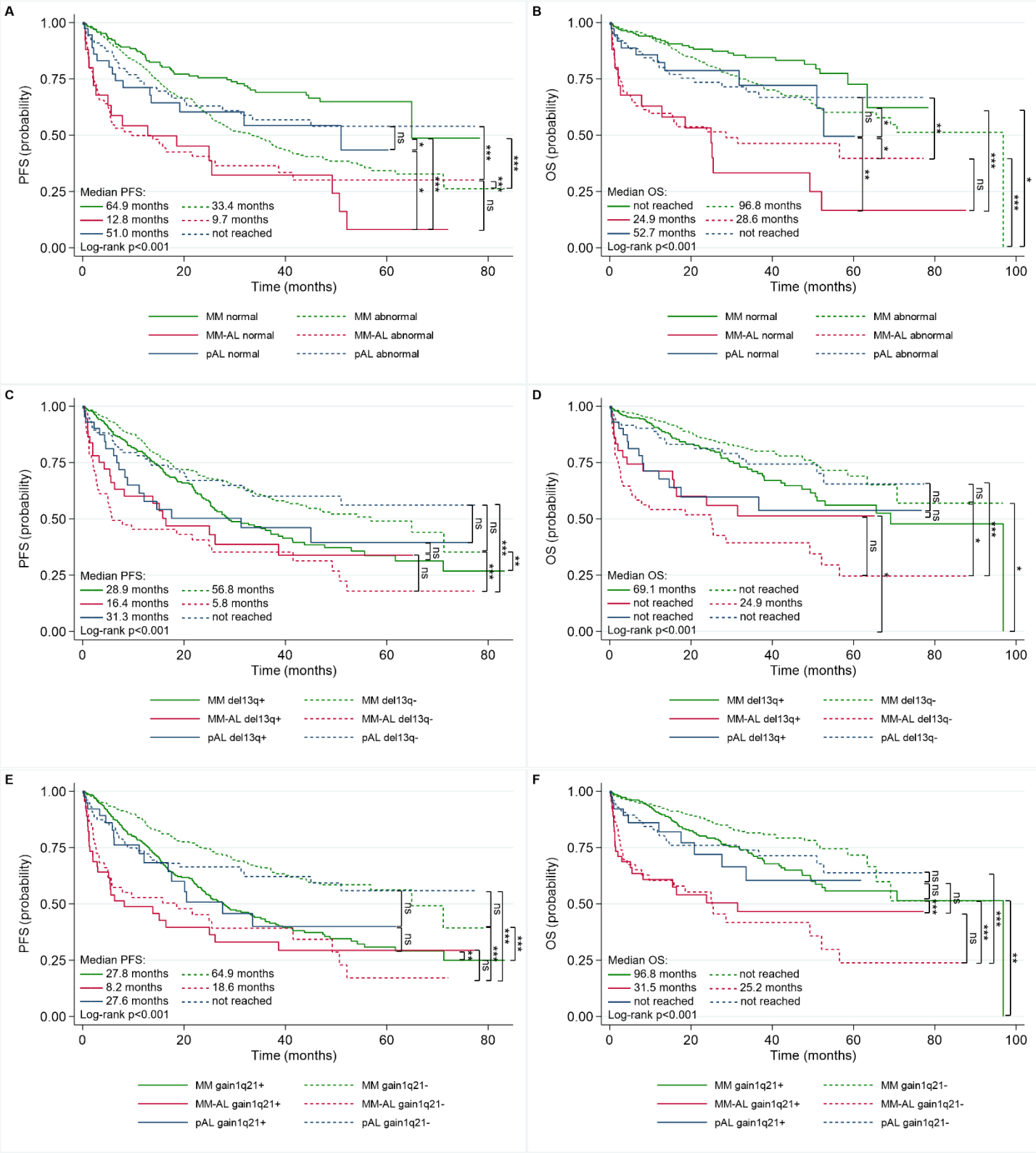
ns, $p \geq 0.05$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$. HRCA, including t(4;14), t(14;16) and del17p.

Supplementary Figure 2 | Association of BMPC levels with cytogenetic abnormalities in patients with MM-AL.



Normal CA group, n= 27; SRCA group, n=26; HRCA group, n=17; gain1q21 group, n=36.
ns, $p \geq 0.05$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. SRCA, standard-risk cytogenetic abnormality, including t(11;14) and del 13q14; HRCA, including t(4;14), t(14;16) and del17p.

Supplementary Figure 3 | Kaplan-Meier curves for progression-free survival and overall survival of patients classified by the type of plasma cell disorders, and by presence of any FISH abnormality (A and B), status of del13q (C and D), and status of gain 1q21 (E and F).



Supplementary Figure 4 | Kaplan-Meier curves for event-free survival (EFS) and overall survival (OS) of patients with MM-AL classified by organ involvement. EFS (A) and OS (B) of patients with and without cardiac involvement. EFS (C) and OS (D) of patients with and without renal involvement. EFS (E) and OS (F) of patients with and without hepatic involvement.

