

Modified carfilzomib dosing is associated with improved treatment responses and longer time on treatment in patients with multiple myeloma

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Supplementary Appendix

Supplementary Table 1: Examples of titration dosing versus standard dosing regimens

Regimen	Standard Dosing	Titration Dosing
Kd (once weekly carfilzomib)	C1D1: K 20mg/m ²	C1D1: K 20mg/m ²
		C1D8: K 27mg/m ²
		C1D15: K 36mg/m ²
		C2D1: K 56mg/m ²
		C2D8: K 70mg/m ² onwards
Kd (twice weekly carfilzomib)	C1D1: K 20mg/m ²	C1D1: K 20mg/m ²
	C1D2: K 20mg/m ²	C1D2: K 27mg/m ²
	C1D8: K 56mg/m ² onwards	C1D8: K 36mg/m ²
		C1D9: K 56mg/m ² onwards
KRd (once weekly carfilzomib)	C1D1: K 20mg/m ²	C1D1: K 20mg/m ²
	C1D8: K 56mg/m ² onwards	C1D8: K 27mg/m ²
		C1D15: K 36mg/m ²
		C2D1: K 56mg/m ² onwards
KCd (twice weekly carfilzomib)	C1D1: K 20mg/m ²	C1D1: K 20mg/m ²
	C1D2: K 20mg/m ²	C1D2: K 20mg/m ²
	C1D8: K 36mg/m ² onwards	C1D8: K 27mg/m ²
		C1D9: K 27mg/m ²
		C1D15: K 36mg/m ² onwards

Abbreviations: Kd – carfilzomib and dexamethasone; KRd – carfilzomib, lenalidomide, and dexamethasone; KCd – carfilzomib, cyclophosphamide, and dexamethasone; CXDY – cycle X, day Y

Supplementary Table 2: Baseline demographic and disease characteristics

	All (n=166)		Titration Dosing (n=36)		Standard Dosing (n=130)		p
	N	%	N	%	N	%	
Age at Diagnosis MM median, range	60	33-87	60	42-71	60	33-87	0.84
Sex							0.15
Female	68	41.0	11	30.6	57	43.8	
Ethnicity							0.24
Caucasian	126	75.9	30	83.3	96	73.8	
CrCl (mL/min) at Start of Tx, median, range	79	8-405	94	24-195	76	8-405	0.01
International Staging System (ISS)							0.46
1	38	22.9	10	32.3	28	28.0	

	2	47	28.3	13	41.9	34	34.0	
	3	46	27.7	8	25.8	38	38.0	
	Unknown	35	21.1	5		30		
Prior Autologous Hematopoietic Cell Transplantation								0.90
Yes	86	51.8	19	52.8	67	51.5		
Prior Immunomodulatory Drugs (IMiD)								0.10
Yes	143	86.1	28	77.8	115	88.5		
Prior Proteasome Inhibitor								0.048
Yes	155	93.4	31	86.1	124	95.4		
Prior Anti-CD38								0.56
Yes	40	24.1	10	27.8	30	23.1		
Prior Cyclophosphamide								0.15
Yes	73	44.0	12	33.3	61	46.9		
Lines of Tx Prior to Carfilzomib median, range	3	0-14	3	0-9	3	0-14		0.79

Supplementary Table 3: Carfilzomib therapy details and treatment responses

Therapy description		All (n=166)		Titration (n=36)		Standard (n=130)		p
		N	%	N	%	N	%	
Therapy description	Doublet (1) or multiple (2) agent							0.50
	1	49	29.5	9	25.0	40	30.8	
	2	117	70.5	27	75.0	90	69.2	
	Front-line (1) or relapsed (2)							0.07
	1	5	3.0	3	8.3	2	1.5	
	2	161	97.0	33	91.7	128	98.5	
Carfilzomib details	Treatment Regimen							0.008
	Carfilzomib + IMiD + dexamethasone	84	50.6	25	29.8	59	70.2	
	Carfilzomib + alkylator + dexamethasone	30	18.1	1	3.3	29	96.7	
	Carfilzomib + other + dexamethasone	3	1.8	1	33.3	2	66.7	
	Carfilzomib + dexamethasone	49	29.5	9	18.4	40	81.6	
	Weekly (1) or twice (2) weekly carfilzomib							0.27
	1	31	18.7	9	25.0	22	16.9	
	2	135	81.3	27	75.0	108	83.1	
	Duration of Treatment							

	Cycles, median, range	4	1-56	7	2-56	3	1-44	<0.001
	Doses, median, range	18	1-162	27.5	8-162	14	1-148	<0.001
	Cumulative Carfilzomib Dose	Median	Range	Median	Range	Median	Range	<0.001
	mg	844	20- 15133	1669	355- 15133	593	20- 8484	
Best response								0.09
	PR or better	76	47.5	23	63.9	53	42.8	
	SD or MR	56	35.0	9	25.0	47	37.9	
	PD	27	16.9	4	11.1	23	18.6	