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Supplementary Materials

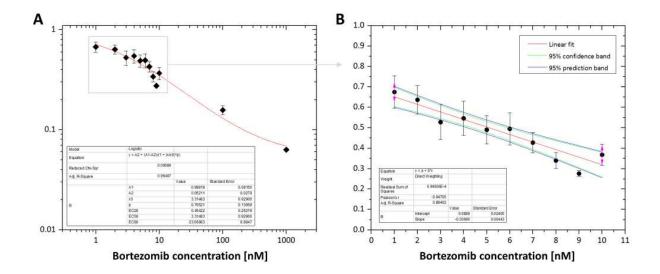


Figure S1. Inhibition of the proteasome activity in RPMI8226 cells by varying concentrations of **bortezomib.** The graph on the left shows the decrease in the fraction of proteasome activity in RPMI8226 cells in response to increasing concentrations of bortezomib treated for 105 minutes. The red curve denotes a fitted curve with an R² value of 0.964. A different, linear curve was fitted to the 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 nM concentrations of bortezomib, shown on the graph on the right. Error bars are SEM with n=3 technical replicates.

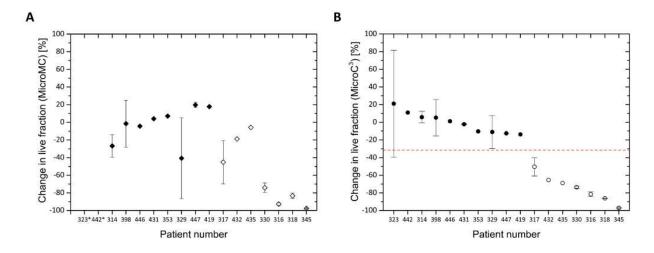


Figure S2. Patient MM tumor cell mean live fraction at 100 nM. The mean live fraction of patient MM tumor cells's *ex vivo* response to 100 nM bortezomib is shown for MicroMC (A) and MicroC³ (B) in descending order of the change in live fraction according to MicroC³. Range bars are shown for those patients for whom technical replicates were/were able to be performed (n=2). Open symbols denote clinically responsive patients whereas solid symbols indicate clinically non-responsive patients. The patients with an asterisk denote those omitted from MicroMC analysis (Pt's 323 and 442). The red line marks the Otsu threshold.

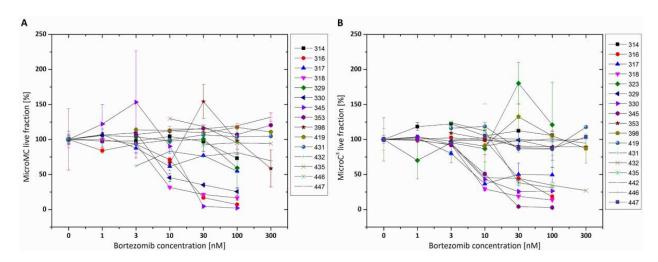


Figure S3. *Ex vivo* **responses of patient MM tumor cells to bortezomib.** *Ex vivo* responses patients' MM cells in MicroMC (A) and MicroC³(B) to bortezomib are shown. Range bars are shown for those patients for whom technical replicates were/were able to be performed (n=2).

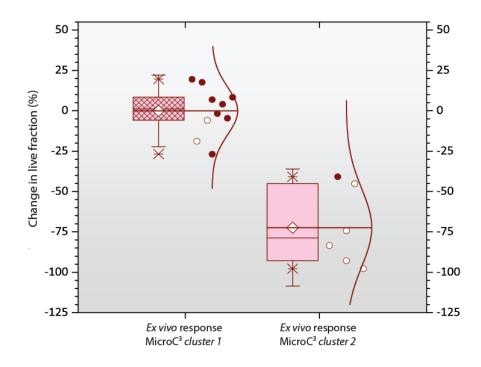


Figure S4. *K*-means clustered *ex vivo* responses of MM patient tumor cells in MicroMC to bortezomib. Box plots of patient *ex vivo* responses in MicroMC (MC) to bortezomib clustered by k-means clustering shown in blue. Open symbols denote clinically responsive patients whereas solid symbols indicate clinically non-responsive patients.

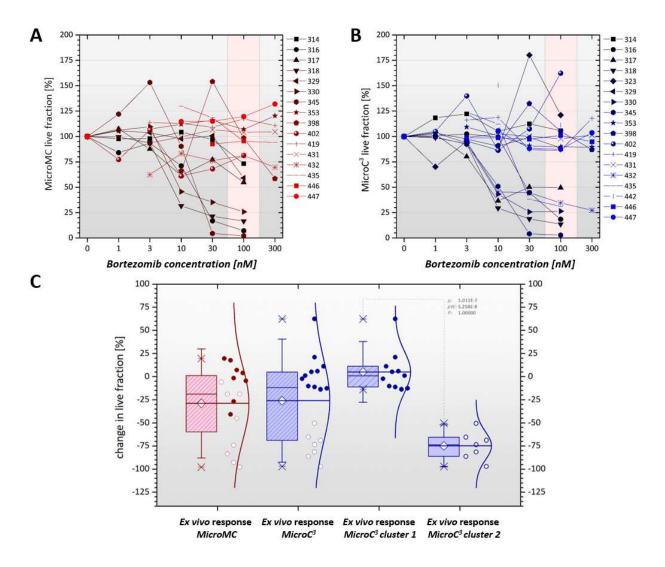


Figure S5. Ex vivo responses of patient MM tumor cells to bortezomib including Pt 402. (A) Ex vivo responses patients' MM cells in MicroMC to bortezomib are shown. (B) Ex vivo responses of patients' MM cells in MicroC³ to bortezomib are shown. C) The first two box plots show patient MM tumor cells' ex vivo responses to bortezomib compared between MicroMC (MC, shown in red) and MicroC³ (shown in blue) (x-axis). The live fraction change is compared between the 0 dose and 100 nM dose of bortezomib (y-axis). K-means and Gaussian clustering methods were applied to MicroC³, resulting in two clusters of the ex vivo cis-cocultured patient MM tumor cells' responses to bortezomib (Cluster 1 and Cluster 2). The same clustering methods applied to MicroMC resulted in one cluster. The two clusters for MicroC³ are shown in blue as the two box plots on the right.

Patient number	Mononuclear cell	Mononuclear cell count after cryo	% alive after cryo	Number of CD138+ cells
142	1,200,000	150,000	12.5%	0
154	1,000,000	200,000	20%	0
321	15,600,000	5,040,000	32.3%	800,000
333	12,800,000	180,000	1.4%	0
334	14,200,000	2,800,000	19.7%	400,000
335	7,840,000	2,000,000	25.5%	80,000
337	3,830,000	1,500,000	39.2%	50,000
345	27,000,000	9,900,000	36.7%	320,000
345 (F)	27,000,000			1,500,000
348	1,900,000	400,000	21.1%	0
378	24,000,000	8,700,000	36.3%	200,000
Average	10,937,000	3,087,000	24.5%	185,000
F,	freshly sort/no cryop	reservation; cryo, cry	yopreservatio	on

Table S1. Patient MM tumor cell counts after cryopreservation.

	Fraction		
	proteasome	Bort	Bort
Time [hr]	activity	[nM]	[ng/mL]
0	0.15719	10	38.424
0.25	0.40456	7.69312	29.56
0.5	0.58288	2.86845	11.02
1	0.65536	0.90736	3.48
2	0.53691	4.11238	15.8
4	0.64557	1.17227	4.5
6	0.5382	4.07738	15.67
8	0.5967	2.49447	9.58
10	0.63714	1.40053	5.39
12	1.00111	-8.44731	0
14	0.85956	-4.61743	0
16	1.08216	-10.6402	0
24	1.17081	-13.0387	0
	AUC	112.9155	

Table S2. Extrapolation of the concentrations of 100 nM bortezomib over 24 hours within $MicroC^3$

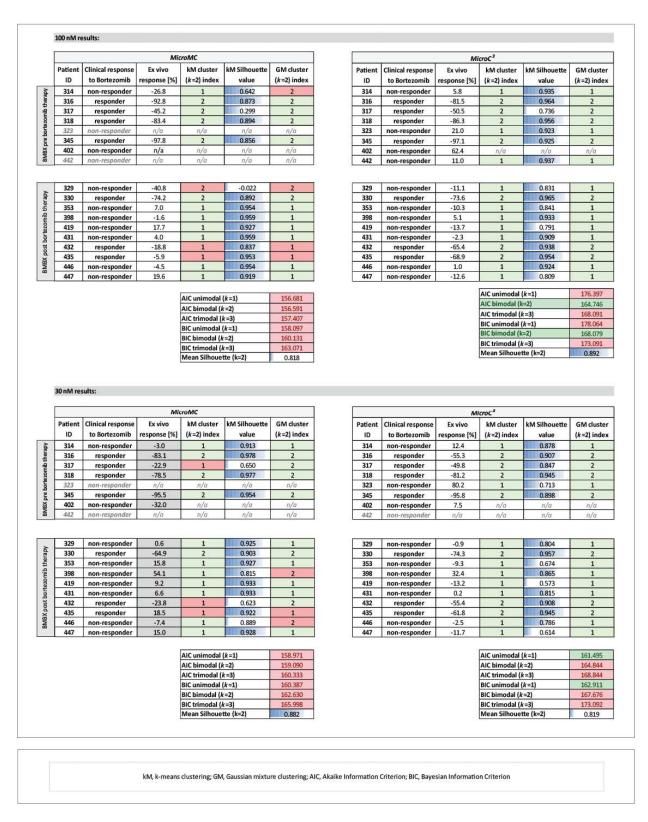


Table S3. K-means and Gaussian mixture model clustering analysis of ex vivo bortezomib sensitivities.

Ī			Mi	roMC			3		AAI	croC ³					
ł	Patient	Clinical response	Ex vivo	kM cluster	kM Silhouette	GM cluster	Patient	Clinical response	Ex vivo	kM cluste	r kM Silhouette	GM cluster	kM cluster	kM Silhouette	GM clus
	ID	to Bortezomib	response [%]	(k=2) index	value	(k=2) index	ID	to Bortezomib	response [%]	(k=2) inde		(k=2) index	(k=3) index	value	(k=3) ind
	314	non-responder	-26.8	1	0.642	1	314	non-responder	5.8	1	0.935	1	1	0.944	1
ı	316	responder	-92.8	2	0.873	2	316	responder	-81.5	2	0.964	2	2	0.957	2
-	317	responder	-45.2	2	0.299	1	317	responder	-50.5	2	0.736	2	2	0.648	2
	318	responder	-83.4	2	0.894	2	318	responder	-86.3	2	0.956	2	2	0.948	2
	323	non-responder	n/a	n/a	n/a	n/a	323	non-responder	21.0	1	0.923	1	1	0.620	1
.	345	responder	-97.8	2	0.856	1	345 402	responder	-97.1 62.4	1	0.925	2	2	0.914	2
	402	non-responder non-responder	-18.8 n/a	n/a	0.838	n/a	402	non-responder non-responder	11.0	1	0.788	1	1	0.890	1
_	712	non-responder	11/0	11/4	11/0	17.0				-		_		3.030	-
	329	non-responder	-40.8	2	-0.022	1	329	non-responder	-11.1	1	0.831	1	1	0.940	1
1	330	responder	-74.2	2	0.892	2	330	responder	-73.6	2	0.965	2	2	0.957	2
İ	353	non-responder	7.0	1	0.954	1	353	non-responder	-10.3	1	0.841	1	1	0.945	1
ı	398	non-responder	-1.6	1	0.959	1	398	non-responder	5.1	1	0.933	1	1	0.948	1
[419	non-responder	17.7	1	0.927	1	419	non-responder	-13.7	1	0.791	1	1	0.917	1
	431	non-responder	4.0	1	0.959	1	431	non-responder	-2.3	1	0.909	1	1	0.967	1
1	432	responder	-18.8	1	0.837	1	432	responder	-65.4	2	0.938	2	2	0.923	2
	435 446	responder non-responder	-5.9 -4.5	1	0.953 0.954	1 1	435 446	responder non-responder	-68.9 1.0	1	0.954	2	2	0.943	2
1	446	non-responder	19.6	1	0.954	1	446	non-responder non-responder	-12.6	1	0.924	1	1	0.964	1
_															
				AIC unimodal	(k=1)	165.902					Analysis with pt 4			alysis without pt	
				AIC bimodal (A		162.990				AIC unimod AIC bimoda		190.606 188.176	AIC unimodal AIC bimodal (I	(K=1)	176.397 164.740
				AIC trimodal (I		168.990				AIC trimoda		183.306	AIC trimodal (168.093
				BIC unimodal		167.447				BIC unimod		192.387	BIC unimodal		178.064
				BIC bimodal (A BIC trimodal (A		166.853 175.170				BIC bimoda		191.737	BIC bimodal (I		168.079
				BIC trimodal (/	(=3)	1/5.1/0				BIC trimoda	144 01				
						0.794						188.648	BIC trimodal (173.09
-	30 nM r	Clinical response	Ex vivo	Mean Silhoue	kM Silhouette	0.784 GM cluster				Mean Silho Patient		0.892	BIC trimodal (i Mean Silhoue		0.909 GM clus
			Ex vivo response [%]	Mean Silhoue	kM Silhouette value					Patient ID	uette (k=2)	0.892 Mi	Mean Silhoue	kM Silhouette	0.909 GM clus
	Patient ID 314	Clinical response to Bortezomib non-responder	Ex vivo response [%]	roMC kM cluster (k=2) index	kM Silhouette value	GM cluster (k=2) index				Patient ID 314	Clinical response to Bortezomib non-responder	0.892 Mi Ex vivo response [%]	kM cluster (k=2) index	kM Silhouette value 0.878	GM clust (k=2) ind
	Patient ID 314 316	Clinical response to Bortezomib non-responder responder	Ex vivo response [%] -3.0 -83.1	romc kM cluster (k=2) index	kM Silhouette value 0.913 0.978	GM cluster (k=2) index				Patient ID 314 316	Clinical response to Bortezomib non-responder responder	0.892 Ex vivo response [%] 12.4 -55.3	kM cluster (k=2) index	kM Silhouette value 0.878 0.907	GM clust (k=2) ind 1
	Patient ID 314 316 317	Clinical response to Bortezomib non-responder responder responder	Ex vivo response [%] -3.0 -83.1 -22.9	croMC kM cluster (k=2) index 1 2	kM Silhouette value 0.913 0.978 0.650	GM cluster (k=2) index 1 2 2				Patient ID 314 316 317	Clinical response to Bortezomib non-responder responder responder	0.892 Mi Ex vivo response [%] 12.4 -55.3 -49.8	kM cluster (k=2) index 1 2	kM Silhouette value 0.878 0.907 0.847	0.909 GM clust (k=2) ind 1 2 2
	Patient ID 314 316	Clinical response to Bortezomib non-responder responder responder responder	Ex vivo response [%] -3.0 -83.1	romc kM cluster (k=2) index	kM Silhouette value 0.913 0.978	GM cluster (k=2) index				Patient ID 314 316 317 318	Clinical response to Bortezomib non-responder responder responder	0.892 Mi Ex vivo response [%] 12.4 -55.3 -49.8 -81.2	Mean Silhoue icro€³ kM cluster (k=2) index 1 2 2	kM Silhouette value 0.878 0.907 0.847 0.945	GM clust (k=2) ind 1
	Patient ID 314 316 317 318	Clinical response to Bortezomib non-responder responder responder	Ex vivo response [%] -3.0 -83.1 -22.9 -78.5	kM cluster (k=2) index 1 2 1 2	kM Silhouette value 0.913 0.978 0.650 0.977	GM cluster (k=2) index 1 2 2 2				Patient ID 314 316 317	Clinical response to Bortezomib non-responder responder responder	0.892 Mi Ex vivo response [%] 12.4 -55.3 -49.8	kM cluster (k=2) index 1 2	kM Silhouette value 0.878 0.907 0.847	0,909 GM clust (k=2) ind 1 2 2
	Patient ID 314 316 317 318 323 345 402	Clinical response to Bortezomib non-responder responder responder responder non-responder non-responder	Ex vivo response [%] -3.0 -83.1 -22.9 -78.5 n/a -95.5 -32.0	Mean Silhoue	kM Silhouette value 0.913 0.950 0.977 n/a 0.275	GM cluster (k=2) index 1 2 2 2 2 n/a 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2				Patient ID 314 316 317 318 323 345 402	Clinical response to Bortezomib non-responder responder responder non-responder non-responder non-responder	0.892 Mi Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5	kM cluster (k=2) index 2 2 1 2 1 1	kM Silhouette value 0.878 0.907 0.847 0.945 0.713 0.898 0.864	0,909 GM clust (k=2) ind 1 2 2 1 2
	Patient ID 314 316 317 318 323 345	Clinical response to Bortezomib non-responder responder responder responder non-responder responder	Ex vivo response [%] -3.0 -83.1 -22.9 -78.5 n/a -95.5	croMC kM cluster (k=2) index 1 2 1 2 n/a 2	kM Silhouette value 0.913 0.978 0.650 0.977 n/a 0.954	GM cluster (k=2) index 1 2 2 2 n/a 2				Patient ID 314 316 317 318 323 345	Clinical response to Bortezomib non-responder responder responder responder responder responder	0.892 Mil Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8	kM cluster (k=2) index 2 2 1 2	kM Silhouette value 0.878 0.907 0.847 0.945 0.713	0,909 GM clus (k=2) inc 1 2 2 1 2
	Patient ID 314 316 317 318 323 345 402 442	Clinical response to Bortezomib non-responder responder responder responder non-responder non-responder non-responder	Ex vivo response [%] -3.0 -83.1 -22.9 -78.5 n/a -95.5 -32.0 n/a	Mean Silhoue	kM Silhouette value 0.913 0.978 0.650 0.977 n/a 0.954 0.275 n/a	GM cluster (k=2) index 1 2 2 2 n/a 2 n/a				Patient ID 314 316 317 318 323 345 402 442	Clinical response to Bortezomib non-responder responder responder non-responder non-responder non-responder	0.892 Min Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5	kM cluster (k=2) index 2 2 1 1 2 1 1 n/a	kM Silhouette value 0.878 0.907 0.847 0.945 0.713 0.898 0.864 n/a	0.909 GM clust (k=2) ind 1 2 2 1 2 1 n/a
1	Patient ID 314 316 317 318 323 345 402 442	Clinical response to Bortezomib non-responder responder responder responder non-responder non-responder non-responder	Ex vivo response [%] -3.0 -83.1 -22.9 -78.5 -78.5 -95.5 -32.0 n/a	Mean Silhoue	kM Silhouette value 0.913 0.978 0.650 0.954 0.275 n/a	GM cluster (k=2) index 1 2 2 2 2 2 n/a 2 1 1 1				Patient 1D 314 316 317 318 323 345 402 442	Clinical response to Bortezomib non-responder responder responder responder non-responder non-responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a	Mean Silhoue	kM Silhouette value 0.878 0.997 0.847 0.945 0.713 0.898 0.864 n/a	0.909 GM clust (k=2) ind 1 2 2 1 2 1 1 1 1
1	Patient ID 314 316 317 318 323 345 402 442	Clinical response to Bortezomib non-responder responder responder responder responder non-responder non-responder non-responder non-responder	Ex vivo response [%] -3.0 -83.1 -22.9 -78.5 n/a -95.5 -32.0 n/a 0.6 -64.9	Mean Silhoue	kM Silhouette value 0.913 0.978 0.650 0.977 n/a 0.275 n/a	GM cluster (k=2) index 1 2 2 2 n/a 2 n/a				Patient ID 314 316 317 318 323 345 402 442	Clinical response to Bortezomib non-responder responder responder non-responder non-responder non-responder	0.892 Mill Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a	kM cluster (k=2) index 2 2 1 1 2 1 1 n/a	kM Silhouette value 0.878 0.907 0.847 0.945 0.713 0.898 0.864 n/a	0.909 GM clust (k=2) ind 1 2 2 1 1 1 1 1
1	Patient ID 314 316 317 318 323 345 402 442	Clinical response to Bortezomib non-responder responder responder responder responder responder responder responder non-responder non-responder non-responder non-responder responder responder responder non-responder non-responder non-responder non-responder	Ex vivo response [%] -3.0 -83.1 -22.9 -78.5 n/a -95.5 -32.0 n/a 0.6 -64.9 15.8	Mean Silhoue	kM Silhouette value 0.913 0.978 0.650 0.977 n/a 0.954 0.275 n/a 0.925 0.993	GM cluster (k=2) index 1 2 2 2 n/a 2 2 n/a 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2				Patient ID 314 316 317 318 323 345 402 442	Clinical response to Bortezomib non-responder responder responder non-responder non-responder non-responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 -95.8 7.5 n/a -0.9 -74.3 -9.3	Mean Silhoue CroC ²	kM Silhouette value 0.878 0.997 0.947 0.713 0.898 0.864 n/0	0.909 GM clust (k=2) ind 1 2 2 2 1 1 0/a 1 1 2 2
1	Patient ID 314 316 317 318 323 345 402 442	Clinical response to Bortezomib non-responder responder responder responder responder non-responder non-responder non-responder non-responder	Ex vivo response [%] -3.0 -83.1 -22.9 -78.5 n/a -95.5 -32.0 n/a 0.6 -64.9	Mean Silhoue	kM Silhouette value 0.913 0.978 0.650 0.977 n/a 0.275 n/a	GM cluster (k=2) index 1 2 2 2 2 2 2 2 2 2 2 1 1 2 2 1 1				Patient ID 314 316 317 318 323 345 402 442	Clinical response to Bortezomib non-responder responder responder non-responder non-responder non-responder	0.892 Mill Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a	Mean Silhoue	kM Silhouette value 0.878 0.907 0.847 0.945 0.713 0.898 0.864 n/a	GM clust (k=2) ind 1 2 2 2 1 1 2 1 2 1 1 0/a
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431	Clinical response to Bortezomib non-responder responder responder responder responder responder responder non-responder	Ex vivo response [%] -3.0 -83.1 -22.9 -78.5 n/a -95.5 -32.0 n/a -95.5 -32.0 s/s -64.9 15.8 54.1 9.2 6.6 6.6	Mean Silhoue	kM Silhouette value 0.913 0.650 0.977 n/a 0.954 0.275 n/a 0.925 0.903 0.927	GM cluster (k=2) index 1 2 2 2 2 n/\(\sigma\) 2 2 2 1 1 1 1 1				Patient ID 314 316 317 318 323 445 402 442 329 330 353 398 419 431	Clinical response to Bortezoniib non-responder responder responder responder responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a -0.9 -74.3 -9.3 32.4 -13.2 0.2	Mean Silhoue	kM Silhouette value 0.878 0.907 0.847 0.913 0.898 0.864 n/a 0.907 0.674 0.985 0.573 0.913 0.913 0.914 0.915	0.909 GM clust (k=2) ind
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432	Clinical response to Bortezomib non-responder responder responder responder responder non-responder responder responder responder responder responder responder	Ex vivo response [%] -3.0 -3.0 -3.1 -22.9 -78.5 -7.0 -95.5 -32.0 -7.0 -95.5 -32.0 -7.0 -64.9 -15.8 -54.1 -9.2 -6.6 -6.2 -3.8	Mean Silhoue	kM Silhouette value 0.913 0.978 0.650 0.997 0.0977 n/a 0.0554 0.225 0.093 0.927 0.0815 0.933 0.933	GM cluster (k=2) index 1 2 2 2 n/a 2 1 2 1 1 2 1 1 2 1 2 1 1 1 1 2				Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432	Clinical response to Bortezomib non-responder responder responder non-responder	0.892 Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a -0.9 -74.3 -9.3 -9.3 -3.2 -0.2 -55.5 -55.4	Mean Silhoue	kM Silhouette value value value 0.878 0.907 0.847 0.907 0.945 0.713 0.896 0.864 n/a 0.804 0.957 0.674 0.885 0.573 0.815 0.933 0.815	0.909 GM clust (k=2) ind 1 2 2 2 1 1 2 1 1 1 2 1 1 1 1 2
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435	Clinical response to Bortezomib non-responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder responder responder responder responder responder responder responder	Ex vivo response [%] -3.0 -3.0 -3.0 -83.1 -22.9 -78.5 -0.70 -9.5 -32.0 -7.6 -9.5 -32.0 -7.6 -64.9 -15.8 -54.1 -9.2 -6.6 -23.8	Mean Silhoue	kM Silhouette value 0.913 0.978 0.0550 0.977 n/0 0.954 0.275 n/0 0.925 0.993 0.927 0.815 0.993 0.993	GM cluster (k=2) index 1 2 2 n/a 2 2 n/a 1 2 1 1 2 1 1 2 1 1 1 1 1				Patient ID 314 316 317 318 323 445 402 442 339 330 353 398 419 431 431 432 435	Clinical response to Bortezomib non-responder responder responder non-responder non-responder non-responder non-responder responder non-responder non-responder non-responder non-responder non-responder non-responder ron-	0.892 Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 -95.8 7.5 -7/4 -0.9 -74.3 -9.3 32.4 -13.2 -0.2 -55.4 -61.8	Mean Silhoue	kM Silhouette value 0.878 0.907 0.847 0.945 0.713 0.998 0.964 n/a 0.957 0.674 0.865 0.573 0.815 0.908 0.945 0.959	0.909 GM clust (k=2) ind
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortezomib non-responder responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder ron-responder responder responder responder responder non-responder	Ex vivo response [%] -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0	Mean Silhoue	kM Silhouette value 0.913 0.650 0.977 n/a 0.954 0.275 n/a 0.925 0.903 0.927 0.815 0.933 0.623 0.922 0.889	GM cluster (k=2) index 1 2 2 2 n/a 2 1 2 1 1 2 1 1 2 1 2 1 1 1 1 2				Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortzomib non-responder responder non-responder responder responder responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a -0.9 -74.3 -9.3 32.4 -13.2 0.2 -55.4 -61.8	Mean Silhoue	kM Silhouette value 0.878 0.907 0.847 0.945 0.713 0.898 0.864 n/o 0.907 0.674 0.985 0.573 0.815 0.908 0.905 0.713 0.905 0.713 0.905 0.713 0.905 0.713 0.905 0.713 0.905 0.713 0.905 0.713 0.908 0.908 0.908 0.908 0.908 0.908	0.909 GM clust (k=2) ind 1 2 2 2 1 1 2 1 1 1 2 1 1 1 1 2
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435	Clinical response to Bortezomib non-responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder responder responder responder responder responder responder responder	Ex vivo response [%] -3.0 -3.0 -3.0 -83.1 -22.9 -78.5 -0.70 -9.5 -32.0 -7.6 -9.5 -32.0 -7.6 -64.9 -15.8 -54.1 -9.2 -6.6 -23.8	Mean Silhoue	kM Silhouette value 0.913 0.978 0.0550 0.977 n/0 0.954 0.275 n/0 0.925 0.993 0.927 0.815 0.993 0.993	$ \begin{array}{c} \text{GM cluster} \\ (k=2) \text{ index} \\ 1 \\ 2 \\ 2 \\ 2 \\ n/\sigma \\ 2 \\ 2 \\ 2 \\ n/\sigma \\ \end{array} $				Patient ID 314 316 317 318 323 445 402 442 339 330 353 398 419 431 431 432 435	Clinical response to Bortezomib non-responder responder responder non-responder non-responder non-responder non-responder responder non-responder non-responder non-responder non-responder non-responder non-responder ron-	0.892 Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 -95.8 7.5 -7/4 -0.9 -74.3 -9.3 32.4 -13.2 -0.2 -55.4 -61.8	Mean Silhoue	kM Silhouette value 0.878 0.907 0.847 0.945 0.713 0.998 0.964 n/a 0.957 0.674 0.865 0.573 0.815 0.908 0.945 0.959	0.909 GM clust (k=2) ind
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortezomib non-responder responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder ron-responder responder responder responder responder non-responder	Ex vivo response [%] -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0	Mean Silhoue	kM Silhouette value 0.913 0.978 0.650 0.977 n/a 0.954 0.275 n/a 0.925 0.933 0.927 0.893 0.923 0.922 0.889	$ \begin{array}{c} \text{GM cluster} \\ (k=2) \text{ index} \\ 1 \\ 2 \\ 2 \\ 2 \\ n/\sigma \\ 2 \\ 2 \\ 2 \\ n/\sigma \\ \end{array} $				Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortzomib non-responder responder non-responder responder responder responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a -0.9 -74.3 -9.3 32.4 -13.2 0.2 -55.4 -61.8	Mean Silhoue	kM Silhouette value value 0.878 0.957 0.945 0.713 0.898 0.804 0.957 0.674 0.895 0.573 0.815 0.965 0.773 0.815 0.965 0.773 0.815 0.968 0.965 0.773 0.815 0.968 0.965 0.778 0.965 0.778 0.815 0.968 0.965 0.778 0.965 0.968 0.965 0.778 0.965 0.968 0.965 0.968 0.965 0.968 0.965 0.778 0.968 0.965 0.968 0.968 0.965 0.968 0.965 0.968 0.965 0.968 0.965 0.968 0.965 0.968 0.965 0.968 0.96	0.909 GM clust (k=2) ind 1 2 2 1 1 2 1 1 2 1 1 1 1 1
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortezomib non-responder responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder ron-responder responder responder responder responder non-responder	Ex vivo response [%] -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0	Mean Silhoue	kM Silhouette value 0.913 0.978 0.650 0.977 n/a 0.954 0.275 n/a 0.925 0.903 0.925 0.933 0.623 0.933 0.623 0.938 0.623 0.929 0.8815	GM cluster (k=2) index 1 2 2 2 2 n/a 2 2 1 2 1 2 1 2 1 2 1 1 2 1 1 1 2 1 1 1 2 1 1 1 2 1 1 1 2 1 1 1 2 1 1 1 2 1 1 1 2 1 1 2 1 1 1 2 1 1 1 2 1 1 1 2 1 1 1 2 1 1 1 2 1 1 1 2 1 1 1 1 2 1 1 1 1 2 1 1 1 1 1 2 1 1 1 1 1 2 1 1 1 1 1 2 1				Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortzomib non-responder responder non-responder responder responder responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a -0.9 -74.3 -9.3 32.4 -13.2 0.2 -55.4 -61.8	Mean Silhoue	kM Silhouette value value value 0.878 0.907 0.847 0.907 0.945 0.713 0.898 0.864 n/o 0.907 0.0545 0.753 0.898 0.957 0.674 0.865 0.573 0.898 0.945 0.806 0.957 0.674 0.865 0.614 (k = 1) v=2)	GM clusts (k=2) infu = 1
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortezomib non-responder responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder ron-responder responder responder responder responder non-responder	Ex vivo response [%] -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0	Mean Silhoue	kM Silhouette value 0.913 0.978 0.650 0.977 n/a 0.954 0.275 n/a 0.993 0.993 0.993 0.992 0.889 0.928 (k=1) 1.55 0.993 0.992 0.889 0.992	GM cluster (k=2) index 1 2 2 n/a 2 2 n/a 2 1 2 1 1 2 1 1 2 1 1 1 1 2 1 1 1 1 2 1 1 1 1 2 1 1 1 1 2 1 1 1 1 2 1 1 1 1 2 1 1 1 2 1 1 1 1 1 2 1 1 1 1 1 2 1 1 1 1 1 2 1 1 1 1 1 2 1 1 1 1 1 2 1 1 1 1 1 2 1 1 1 1 1 1 2 1				Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortzomib non-responder responder non-responder responder responder responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a -0.9 -74.3 -9.3 32.4 -13.2 0.2 -55.4 -61.8	Mean Silhoue	kM Silhouette value value 0.878 0.907 0.945 0.713 0.898 0.864 0.997 0.674 0.865 0.573 0.815 0.998 0.995 0.674 0.865 0.573 0.815 0.998 0.945 0.786 0.614 (k=1)	0.909 GM clust (k=2) ind in (k=2) ind in (k=2) ind in (k=2) ind in (k=2) i
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortezomib non-responder responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder ron-responder responder responder responder responder non-responder	Ex vivo response [%] -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0	Mean Silhoue	kM Silhouette value 0.913 0.978 0.650 0.977 n/a 0.954 0.275 n/a 0.925 0.993 0.927 0.815 0.993 0.927 0.815 0.993 0.922 0.889 0.928	GM cluster (k=2) index 1 2 2 2 2 n/\sigma 2 2 2 1 1 2 2 1 1 1 1 2 2 1 1 1 1 1 1				Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortzomib non-responder responder non-responder responder responder responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a -0.9 -74.3 -9.3 32.4 -13.2 0.2 -55.4 -61.8	Mean Silhoue	kM Silhouette value 0.878 0.0878 0.097 0.847 0.945 0.713 0.898 0.864 0.70 0.804 0.957 0.674 0.885 0.573 0.815 0.098 0.815 0.098 0.411 0.866 0.614	0.909 GM clust (k=2) ind in (k=2) ind in (k=2) ind in (k=2) ind in (k=2) i
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortezomib non-responder responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder ron-responder responder responder responder responder non-responder	Ex vivo response [%] -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0	Mean Silhoue	kM Silhouette value 0.913 0.978 0.650 0.977 n/a 0.954 0.275 n/a 0.927 0.933 0.927 0.815 0.933 0.922 0.839 0.922 0.889 0.828	GM cluster (k=2) index 1 2 2 2 1/a 2 2 1 2 1 2 1 2 1 1 2 1 1 1 2 1 1 1 1				Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortzomib non-responder responder non-responder responder responder responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a -0.9 -74.3 -9.3 32.4 -13.2 0.2 -55.4 -61.8	Mean Silhoue	kM Silhouette value 0.87% 0.907 0.945 0.713 0.89% 0.957 0.674 0.955 0.573 0.815 0.905 0.91	GM clust (k=2) ind
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortezomib non-responder responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder ron-responder responder responder responder responder non-responder	Ex vivo response [%] -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0	Mean Silhoue	kM Silhouette value 0.913 0.978 0.0550 0.977 n/0 0.954 0.275 n/0 0.925 0.903 0.927 0.815 0.993 0.623 0.922 0.889 0.928	GM cluster (k=2) index 1 2 2 2 2 n/a 2 2 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1				Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortzomib non-responder responder non-responder responder responder responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a -0.9 -74.3 -9.3 32.4 -13.2 0.2 -55.4 -61.8	Mean Silhoue	kM Silhouette value 0.878 0.977 0.947 0.945 0.713 0.898 0.864 0.957 0.674 0.865 0.573 0.815 0.796 0.614 (k=1) (k=2) (k=3)	GM clus (k=2) ind (k=2) in
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortezomib non-responder responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder ron-responder responder responder responder responder non-responder	Ex vivo response [%] -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0	Mean Silhoue	kM Silhouette value 0.913 0.978 0.0550 0.977 n/0 0.954 0.275 n/0 0.925 0.903 0.927 0.815 0.993 0.623 0.922 0.889 0.928	GM cluster (k=2) index 1 2 2 2 1/a 2 2 1 2 1 2 1 2 1 1 2 1 1 1 2 1 1 1 1				Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortzomib non-responder responder non-responder responder responder responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a -0.9 -74.3 -9.3 32.4 -13.2 0.2 -55.4 -61.8	Mean Silhoue	kM Silhouette value 0.878 0.977 0.947 0.945 0.713 0.898 0.864 0.957 0.674 0.865 0.573 0.815 0.796 0.614 (k=1) (k=2) (k=3)	GM clus (k=2) ind
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortezomib non-responder responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder ron-responder responder responder responder responder non-responder	Ex vivo response [%] -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0	Mean Silhoue	kM Silhouette value 0.913 0.978 0.0550 0.977 n/0 0.954 0.275 n/0 0.925 0.903 0.927 0.815 0.993 0.623 0.922 0.889 0.928	GM cluster (k=2) index 1 2 2 2 2 n/a 2 2 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1				Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortzomib non-responder responder non-responder responder responder responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a -0.9 -74.3 -9.3 32.4 -13.2 0.2 -55.4 -61.8	Mean Silhoue	kM Silhouette value 0.878 0.977 0.947 0.945 0.713 0.898 0.864 0.957 0.674 0.865 0.573 0.815 0.796 0.614 (k=1) (k=2) (k=3)	GM clus (k=2) ind (k=2) in
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortezomib non-responder responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder ron-responder responder responder responder responder non-responder non-responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder	Ex vivo response [%] -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0	Mean Silhoue	kM Silhouette value 0.913 0.978 0.0550 0.977 n/0 0.954 0.275 n/0 0.925 0.903 0.927 0.815 0.993 0.623 0.922 0.889 0.928	GM cluster (k=2) index 1 2 2 2 2 n/a 2 2 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1				Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortzomib non-responder responder non-responder responder responder responder non-responder	0.892 MM Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 7.5 n/a -0.9 -74.3 -9.3 32.4 -13.2 0.2 -55.4 -61.8	Mean Silhoue	kM Silhouette value 0.878 0.977 0.947 0.945 0.713 0.898 0.864 0.957 0.674 0.865 0.573 0.815 0.796 0.614 (k=1) (k=2) (k=3)	GM clus (k=2) ind (k=2) in
	Patient ID 314 316 317 318 323 345 402 442 329 330 353 398 419 431 432 435 446	Clinical response to Bortezomib non-responder responder responder responder responder responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder ron-responder responder responder responder responder non-responder non-responder responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder non-responder	Ex vivo response [%] -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0 -3.0	Mean Silhoue	kM Silhouette value 0.913 0.978 0.0550 0.977 n/0 0.954 0.275 n/0 0.925 0.903 0.927 0.815 0.993 0.992 0.889 0.928 (k=1) ==2) k=3) [k=1] ==2) tte (k=2)	GM cluster (k=2) index 1 2 2 2 2 n/\(\sigma\) 2 2 2 1 1 2 2 1 1 2 2 1 1 1 1 2 2 1	xture dusterino	; AIC, Akaike Infon		Patient ID 314 316 317 318 323 345 402 442 431 431 431 435 446 447	Clinical response to Bortezomib non-responder responder responder non-responder responder non-responder non-respon	0.892 Ex vivo response [%] 12.4 -55.3 -49.8 -81.2 80.2 -95.8 -7.5 -7/a -0.9 -74.3 -9.3 32.4 -13.2 0.2 -55.4 -61.8 -2.5 -11.7	Mean Silhoue	kM Silhouette value 0.878 0.977 0.947 0.945 0.713 0.898 0.864 0.957 0.674 0.865 0.573 0.815 0.796 0.614 (k=1) (k=2) (k=3)	GM cluster 1

Table S4. K-means and Gaussian mixture model clustering analysis of $ex\ vivo$ bortezomib sensitivities, including Pt 402.