

Supplementary Table S1. Summary of the multivariable Cox regression models based on dataset GSE4581 [Zhan et al, Blood 2006] for the effect of DSG2 expression on overall survival

Cox Model	Model Covariates	Hazard Ratio	95% Confidence Interval	p value
Model 1 (all patients)	<ul style="list-style-type: none"> • DSG2 expression level 	2.69	1.73 – 4.18	< 0.001
Model 2 (all patients)	<ul style="list-style-type: none"> • DSG2 expression level • Genetic subgroup 	3.03	1.75 – 5.25	< 0.001
Model 3 (non-MS cohort)	<ul style="list-style-type: none"> • DSG2 expression level • MS cohort 	3.68	2.18 – 6.22	< 0.001
Model 4 (all patients)	<ul style="list-style-type: none"> • DSG2 expression level • MS cohort • Therapy 	4.30	2.47 – 7.48	< 0.001

Supplementary Table S2. The effect DSG2 expression on patient overall survival in each genetic subgroup using dataset GSE4581 and univariable Cox regression modelling

	Genetic Grouping	Prognostic Significance	DSG2 (high/low)	Hazard Ratio	95% Confidence Interval	p value	Adjusted Confidence Interval (99%)	Adjusted p value
CD-1 (n=28)	Cyclin D1 and cyclin D3: t(11;14) and t(6;14)	Low-risk	5 / 23	6.60	0.91 – 47.56	0.06	0.49 – 88.46	0.37
CD-2 (n=59)	Cyclin D1 and cyclin D3: t(11;14) and t(6;14)	Low-risk	12 / 48	0.62	0.07 – 5.18	0.66	0.04 – 10.07	4.00
HY (n=116)	Hyperdiploidy	Low-risk	12 / 104	3.21	1.04 – 9.92	0.04	0.73 – 14.14	0.26
LB (n=58)	Low bone disease	Low-risk	4 / 54	9.08	1.65 – 50.13	0.01	0.96 – 85.75	0.07
MF (n=37)	MAF: t(14;16) and t(14;20)	High-risk	9 / 28	8.76	1.70 – 45.20	0.01	1.01 – 75.70	0.06
MS (n=68)	MMSET: t(4;14)	High-risk	66 / 2	Indeterminate	Indeterminate	Indeterminate		
PR (n=47)	Proliferation related	High-risk	17 / 30	2.00	0.79 – 5.11	0.15	0.59 – 6.85	0.87

Supplementary Table S3. Multivariable Cox regression model of the coMMpass study data for progression-free survival by DSG2 expression level and frontline therapy

Therapy	Median PFS (months)		Multivariable Cox Regression (<i>DSG2-high</i> vs <i>DSG2-low</i>)
	<i>DSG2-low</i>	<i>DSG2-high</i>	
<i>Bortezomib</i>	22	15	HR 1.49, CI 1.10 – 2.03, P = 0.01
<i>Carfilzomib</i>	NR	26	HR 2.41, CI 0.64 – 9.10, P = 0.19
<i>Lenalidomide</i>	21	22	HR 1.20, CI 0.67 – 2.13, P = 0.55

Supplementary Table S4. Multivariable Cox regression model of the coMMpass study data for overall survival by DSG2 expression level and frontline therapy

Therapy	Median OS (months)		Multivariable Cox Regression (<i>DSG2-high</i> vs <i>DSG2-low</i>)
	<i>DSG2-low</i>	<i>DSG2-high</i>	
<i>Bortezomib</i>	58	36	HR 1.86, CI 1.27 – 2.71, P < 0.01
<i>Carfilzomib</i>	NR	NR	HR 1.17, CI 0.20 – 7.04, P = 0.86
<i>Lenalidomide</i>	60	61	HR 1.00, CI 0.41 – 2.38, P = 0.99

Supplementary Table S5. Correlation of DSG2 expression on patient MM PC against routinely measured blood parameters.

Biomarker	Linear Regression (p value)	Pearson Correlation (r value, p value)
Paraprotein	0.151	- 0.091, 0.543
κ light chain	0.549	- 0.090, 0.549
λ light chain	0.488	0.104, 0.488
κ : λ ratio	0.655	-0.067, 0.655
Haemoglobin	0.131	- 0.224, 0.131
White cell count	0.518	0.097, 0.518
Platelet count	0.700	0.058, 0.700
β_2 -microglobulin	0.425	-0.027, 0.860
Urea	0.738	0.051, 0.738
Creatinine	0.558	0.088, 0.558
Calcium	0.929	-0.013, 0.929
Albumin	0.143	-0.217, 0.143
Lactate dehydrogenase	0.168	-0.135, 0.365
Plasma cell percentage (marrow aspirate)	0.154	-0.055, 0.716
Plasma cell percentage (CD138 ⁺ IHC of trephine)	0.442	-0.145, 0.331