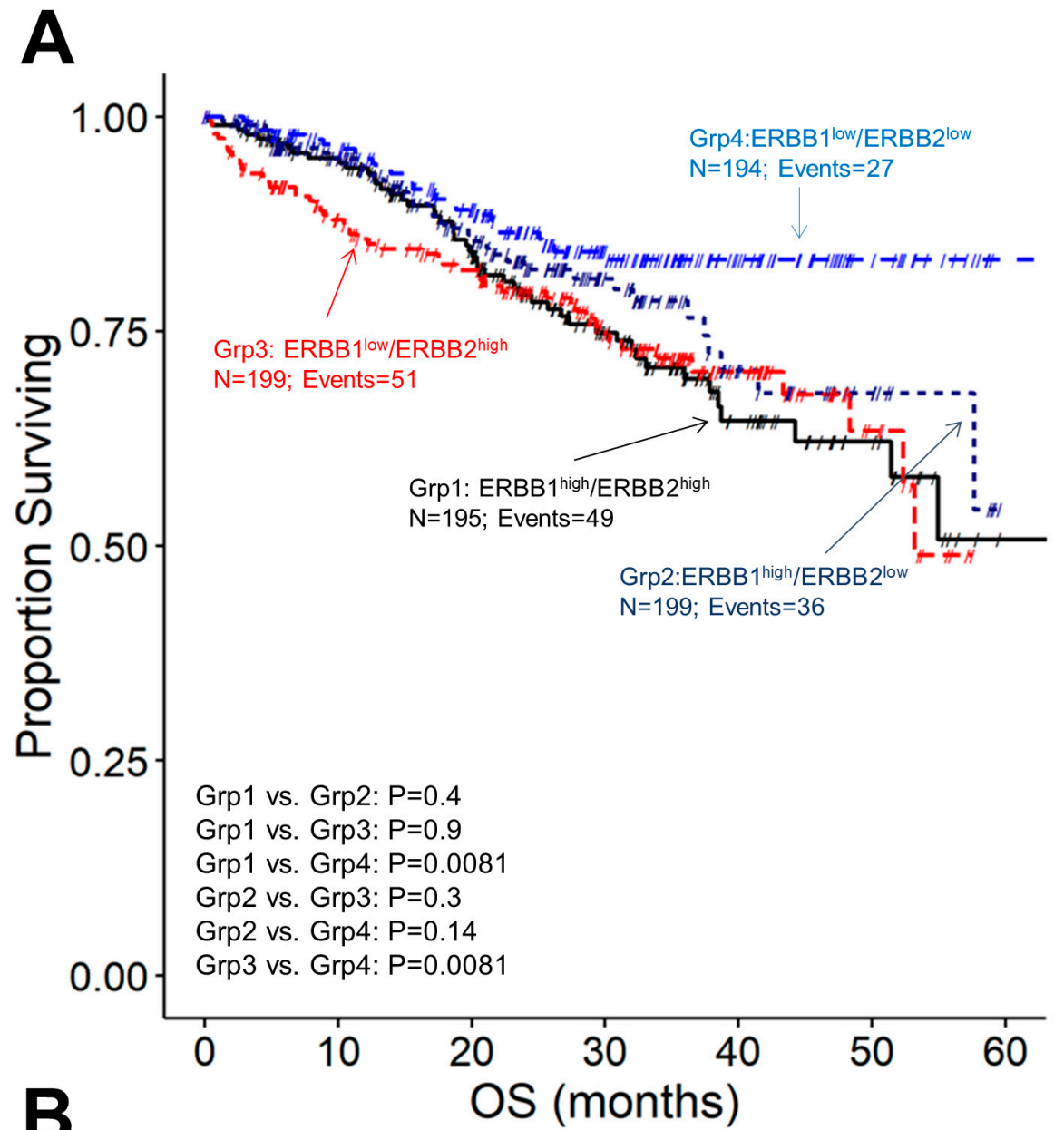


Figure S1. Higher expression levels of ERBB2/HER2 in malignant plasma cells from MM patients is associated with shorter PFS

[A] Depicted for comparison are the PFS curves (censored at 48 months) for 335 ERBB2^{high} MM patients (i.e., patients with the top 50% of the highest observed expression level for FPKM-UQ aligned to the ERBB2 sequence) and 334 ERBB2^{low} MM patients (i.e., 334 patients bottom 50% with the lowest observed expression level for FPKM-UQ aligned to the ERBB2 sequence). Cumulative proportion surviving progression-free at 48 mo: $31.1 \pm 2.9\%$ for ERBB2^{high} and $35.9 \pm 3.1\%$ for ERBB2^{low}. **[B]** Depicted is the Forest plot comparing the HRs for each covariate included in a multivariate Cox proportional hazards model, namely ERBB2 mRNA level, ISS stage, age, as well as serum albumin and beta 2 microglobulin levels. ERBB2 mRNA expression level exhibited a significant 1.54-fold increase in the hazard ratio for each unit increase in FPKM-UQ counts ($P < 0.001$). Significant p-values are indicated by *, ** and *** for $p < 0.05$, $p < 0.01$ and $p < 0.001$ respectively.



Group	ERBB1/ERBB2 expression	N	#Events	Median	Lower 95% CI	Upper 95% CI	Cumulative surviving at 60 months (%)
Grp1	ERBB1 ^{high} /ERBB2 ^{high}	195	49	>60 mo	51.4	NA	50.8 ± 9
Grp2	ERBB1 ^{high} /ERBB2 ^{low}	199	36	>60 mo	57.7	NA	54.3 ± 12.9
Grp3	ERBB1 ^{low} /ERBB2 ^{high}	199	51	53.2 mo	52.3	NA	48.9 ± 10
Grp4	ERBB1 ^{low} /ERBB2 ^{low}	194	27	>60 mo	NA	NA	83.3 ± 3

Figure S2. The prognostic impact of ERBB1 and ERBB2 on Overall Survival (OS) in newly diagnosed MM patients from the MMRF-CoMMpass study. [A] Depicted for comparison are the OS curves for 4 distinct patient groups defined by co-expression levels of ERBB2 and ERBB1: (i)

ERBB1^{high}/ERBB2^{high} (top 50th percentile of the highest observed expression levels for both ERBB1 and ERBB2 mRNA expression levels) (N=195), (ii) ERBB1^{low}/ERBB2^{low} (bottom 50th percentile of the lowest observed expression levels for both ERBB1 and ERBB2 (N=194), (iii) ERBB1^{low}/ERBB2^{high} (N=199) and (iv) ERBB1^{high}/ERBB2^{low}(N=199). [**B**] ERBB1^{low}/ERBB2^{low} patients (Grp4) had fewer deaths and the best 5-year survival of 83.3%.

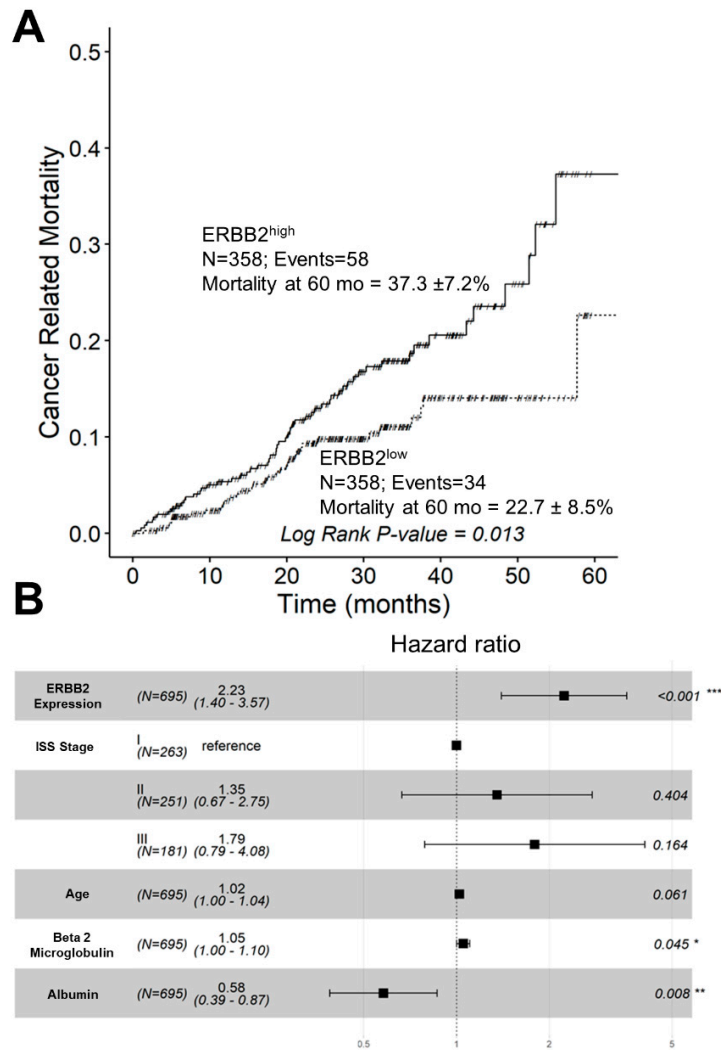


Figure S3. Amplified expression of ERBB2 is associated with increased cancer-related mortality (CRM) in newly diagnosed MM patients from the MMRF-CoMMpass study.

[A] Depicted for comparison are the CRM curves (censored at 60 months) for 358 ERBB2^{high} patients (i.e., patients with the top 50% of the highest observed expression level for FPKM-UQ aligned to the ERBB2 sequence) and 358 ERBB2^{low} patients (i.e., patients bottom 50% with the lowest observed expression level for FPKM-UQ aligned to the ERBB2 sequence). **[B]** Depicted is the Forest plot comparing the HRs for each covariate included in a multivariate Cox proportional hazards model, namely ERBB2 mRNA level, ISS stage, age, as well as serum albumin and beta 2 microglobulin levels. ERBB2 mRNA expression level exhibited a significant 2.23-fold increase in the hazard ratio for each unit increase in FPKM-UQ counts ($P < 0.001$). Significant P-values are indicated by *, ** and *** for $p < 0.05$, $p < 0.01$ and $p < 0.001$ respectively.

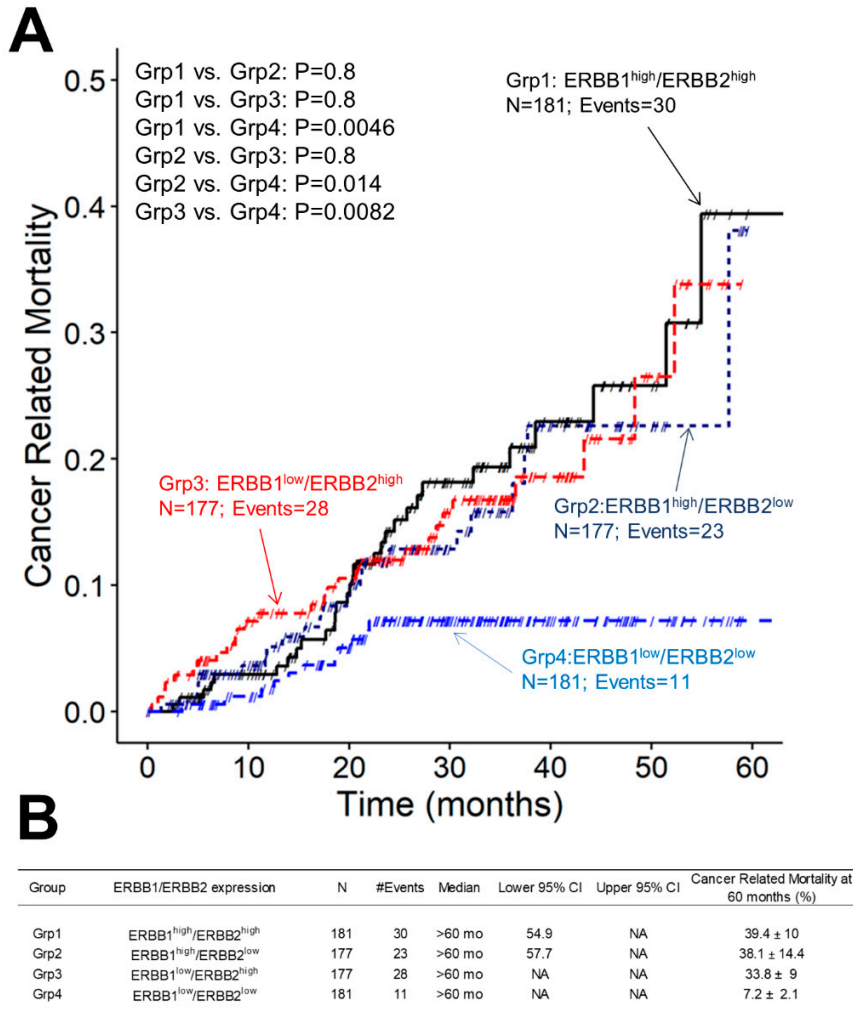


Figure S4. The prognostic impact of ERBB1 and ERBB2 on cancer-related mortality (CRM) in newly diagnosed MM patients from the MMRF-CoMMpass study.

[A] Depicted for comparison are the CRM curves for 4 distinct patient groups defined by co-expression levels of ERBB2 and ERBB1: (i) ERBB1^{high}/ERBB2^{high} (top 50th percentile of the highest observed expression levels for both ERBB1 and ERBB2 mRNA expression levels) (N=181), (ii) ERBB1^{low}/ERBB2^{low} (bottom 50th percentile of the lowest observed expression levels for both ERBB1 and ERBB2 (N=181) , (iii) ERBB1^{low}/ERBB2^{high} (N=177) and (iv) ERBB1^{high}/ERBB2^{low}(N=177). [B] ERBB1^{low}/ERBB2^{low} patients representing 25.3% of the 716 evaluable patients had significantly fewer cancer-related deaths consequently the lowest 5-year CRM (7.2±2.1%) when compared to the remaining 3 groups of patients (5-year CRM: ERBB1^{high}/ERBB2^{high} = 39.4 ± 10%, ERBB1^{high}/ERBB2^{low} = 38.1 ± 14.4%, ERBB1^{low}/ERBB2^{high} = 33.8 ± 9%).