

List of Supplementary Materials

Supplementary Tab 1. Patient demographic, disease characteristics and therapy

Supplementary Fig.1: Pie chart patients' diagnosis

Supplementary Fig. 2: Box charts of iron transporter expression profiles show dysregulation between normal plasma cells and MM cells. The 22 normal plasma cell (NPC), 44 MGUS, and 351 newly diagnosed MM samples are distributed along the x-axis and the log₂-transformed Affymetrix Signal is plotted on the y-axis. The top, bottom, and middle lines of each box correspond to the 75th percentile (top quartile), 25th percentile (bottom quartile), and 50th percentile (median) of the log₂-transformed Affymetrix Signal for each gene, respectively. The whiskers extend from the 10th percentile (bottom decile) and top 90th percentile (top decile). The One-Way ANOVA tests for differences in expression of each gene across the groups are: *TfR1*, $p < 0.001$; *FPN1*, $p < 0.001$.

Supplementary Fig. 3: Combination of PAA with melphalan does not change body weight. Six groups of ARP1 xenografted NOD.Cγ-Rag1 mice were treated with PAA and with or without melphalan (1, 3, and 5 mg/kg) and body weight was determined at the specified time.

Supplementary Fig. 4: Combination of PAA with melphalan increases MM mouse survival. An IVIS shows ARP1 cell growth in xenografted NOD.Cγ-Rag1 mice with or without PAA treatment (4 g/kg, i.p. once a day, 5 days a week for 3 weeks). Total flux after PAA treatment was normalized with pre-PAA treatment and indicates quantification of luciferase intensity of mice post-PAA treatment. ARP1 xenografted NOD.Cγ-Rag1 mice were treated with PAA or melphalan alone or in combination (1, 3, and 5 mg/kg). Total flux indicates quantification of luciferase intensity of mice pre- and post-PAA treatment at different time points.

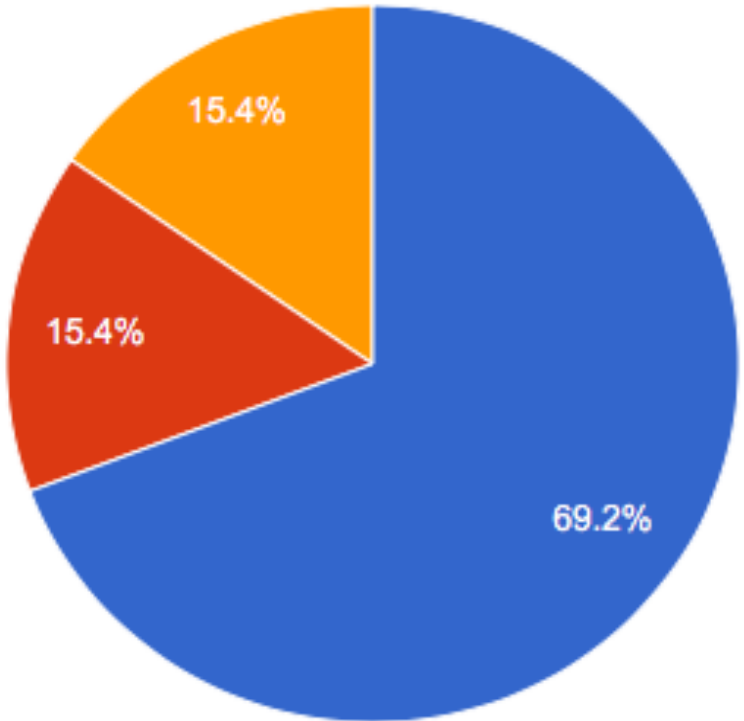
Supplementary Fig. 5: BCS does not block PAA anti-cancer activity. (A) OCI-MY5 EV and OE cells were incubated with or without BCS (10 μM) for 3 hrs following PAA treatment (4 mM). PAA was washed away after 1 hr and cell viability was determined 24 hrs later. (B) Total RNA was extracted from OCI-MY5 EV and OE cells and *Fpn1* mRNA was analyzed by Real time RT-PCR.

Supplementary Fig. 6: Pan-caspase inhibitor decreases PAA sensitivity. OCI-MY5 WT cells were incubated with or without Q-VD-OPh for 6 hrs following treatment with PAA. PAA was washed away after 1 hr treatment and cell viability was determined 24 hrs later.

Supplementary Tab1

Subject	Disease	Age	Sex	M-component type	Stage (ISS)	Plasma Cells (%)	Cytogenetics	Last treatment
1	MGUS	58	F	IgA Kappa	nd	5.0	Hyperdiploid karyotype p53 amplification	NT
3	MM	65	M	IgG Kappa	I	20	Hyperdiploid karyotype	D-PACE
4	MM	38	M	IgG Kappa	II	2.0	Hyperdiploid karyotype	Carfilzomib Dexamethasone Lenalidomide
5	MM	62	F	IgG Lambda	I	4.0	1q amplification t (14;16) (q32;q23)	Melphalan VTD
6	MM	62	M	IgG Lambda	III	80	Hypodiploid karyotype 1q amplification	VDT
7	MM	79	F	IgG Kappa	III	10	1q amplification p53 amplification t (4;14) (p16;q32)	Dexamethasone Lenalidomide
8	MM	59	M	IgG Lambda	II	5.0	1q amplification t (4;14) (p16;q32)	Bortezomib Lenalidomide
9	MM	56	F	Lambda Light Chain ONLY	II	<1	Hypodiploid karyotype	RVD
11	SMM	48	M	IgA Kappa	nd	6.0	Hypodiploid karyotype 1q amplification t (4;14) (p16;q32)	NT
12	SMM	60	M	IgG Lambda	nd	15	Hypodiploid karyotype 1q amplification	NT
13	MM	49	F	IgA Lambda	II	60	Hyperdiploid karyotype	Bortezomib Dexamethasone
14	MGUS	65	F	IgG Lambda	nd	5	Normal FISH	NT
15	MM	61	F	IgG Kappa	I	17	13q deletion 1q amplification t (11;14) (q13;q32)	Bortezomib Dexamethasone

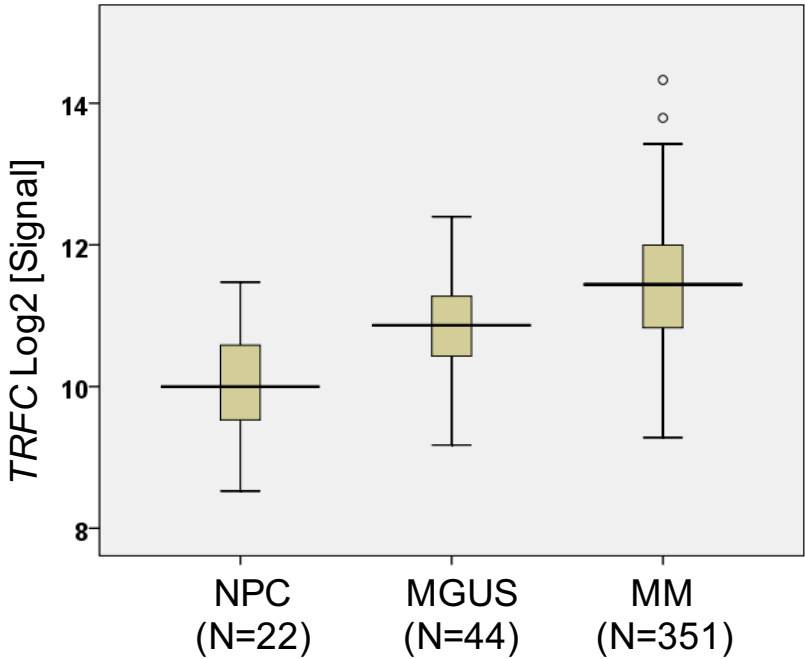
Supplementary Fig. 1



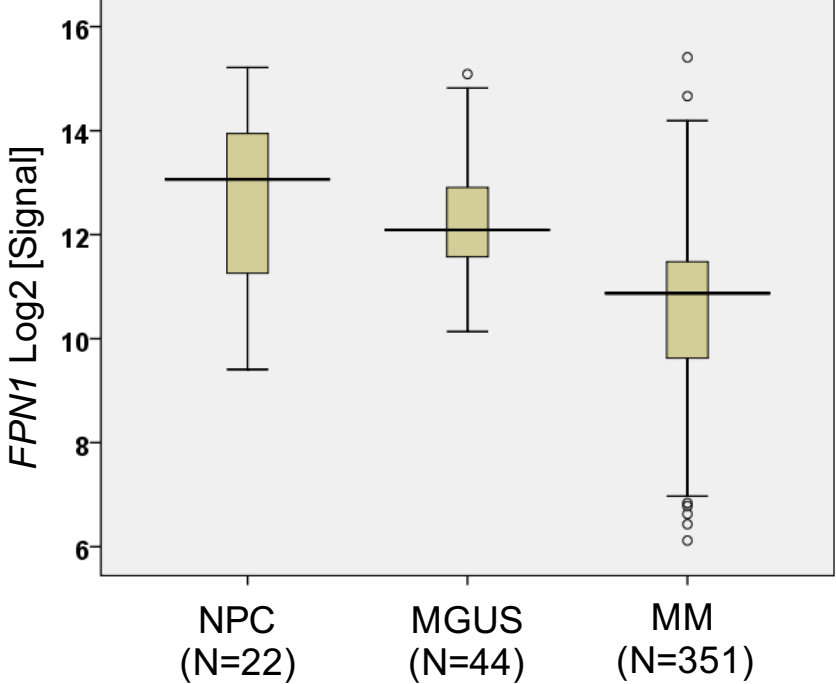
Multiple Myeloma (9, 69.2%), MGUS (2, 15.4%), Smoldering Myeloma (2, 15.4%)

Supplementary Fig. 2

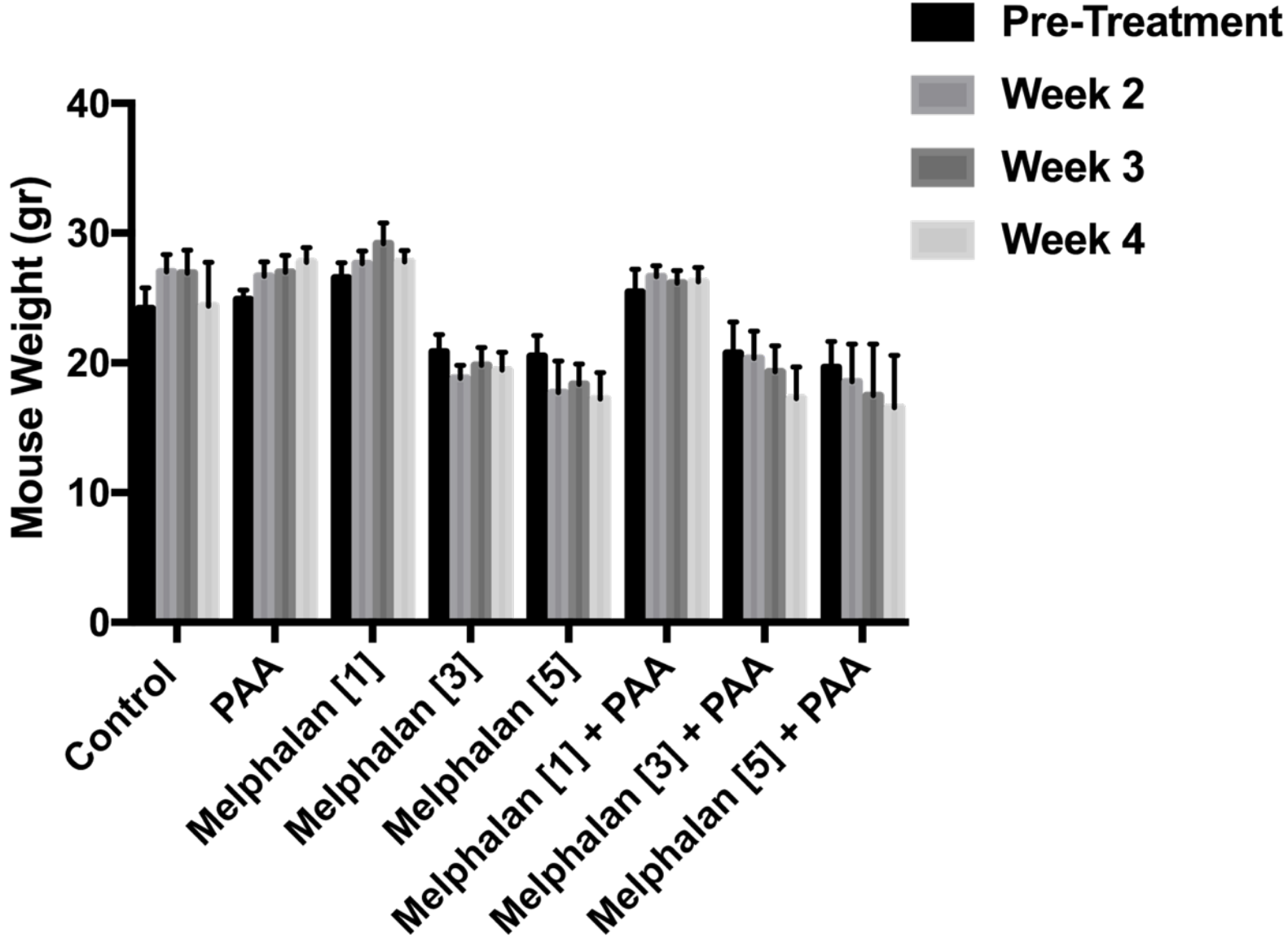
A



B

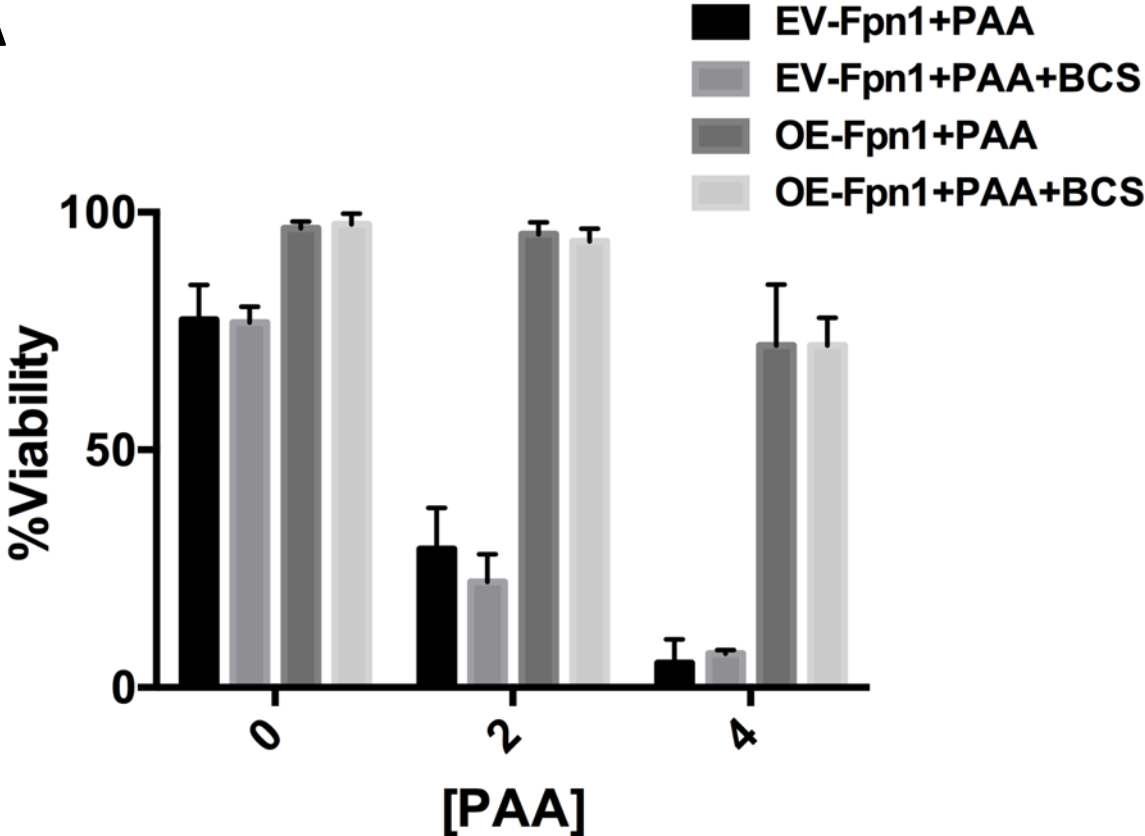


Supplementary Fig. 3

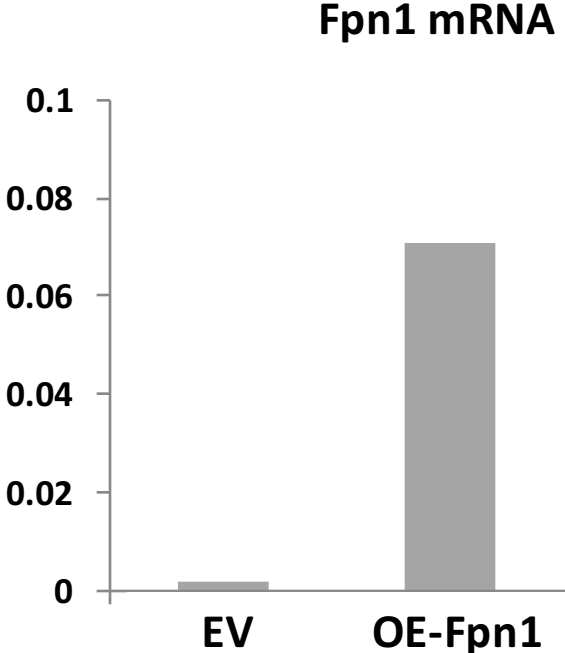


Supplementary Fig. 5

A



B



Supplementary Fig. 6

