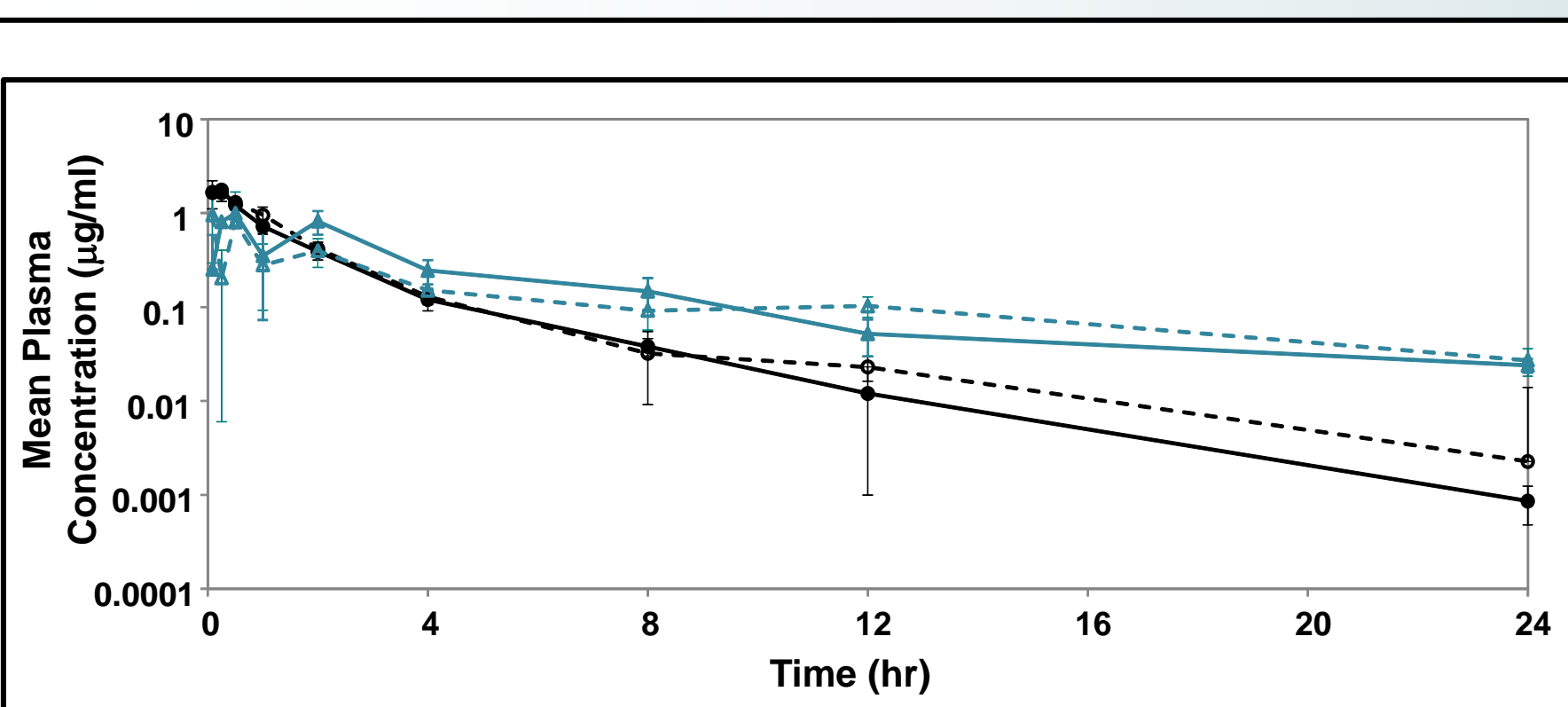


## Introduction

- ARRAY-520 is a selective Kinesin Spindle Protein (KSP) inhibitor
  - KSP is a mitosis-specific motor protein
  - Inhibition of KSP causes aberrant mitotic arrest and subsequent apoptosis
- ARRAY-520 is in Phase 2 clinical studies in patients with relapsed and refractory multiple myeloma (MM)
  - Clinical activity and acceptable safety have been observed both alone and in combination with bortezomib, dexamethasone, or carfilzomib
- ARRAY-520 is additive or synergistic when combined with bortezomib in several preclinical *in vivo* models of MM
- Combinability of ARRAY-520 with other MM standards of care, such as immunomodulatory drugs, has not been thoroughly investigated
- Here we have evaluated the combination utility of ARRAY-520 and pomalidomide in preclinical *in vivo* models of MM

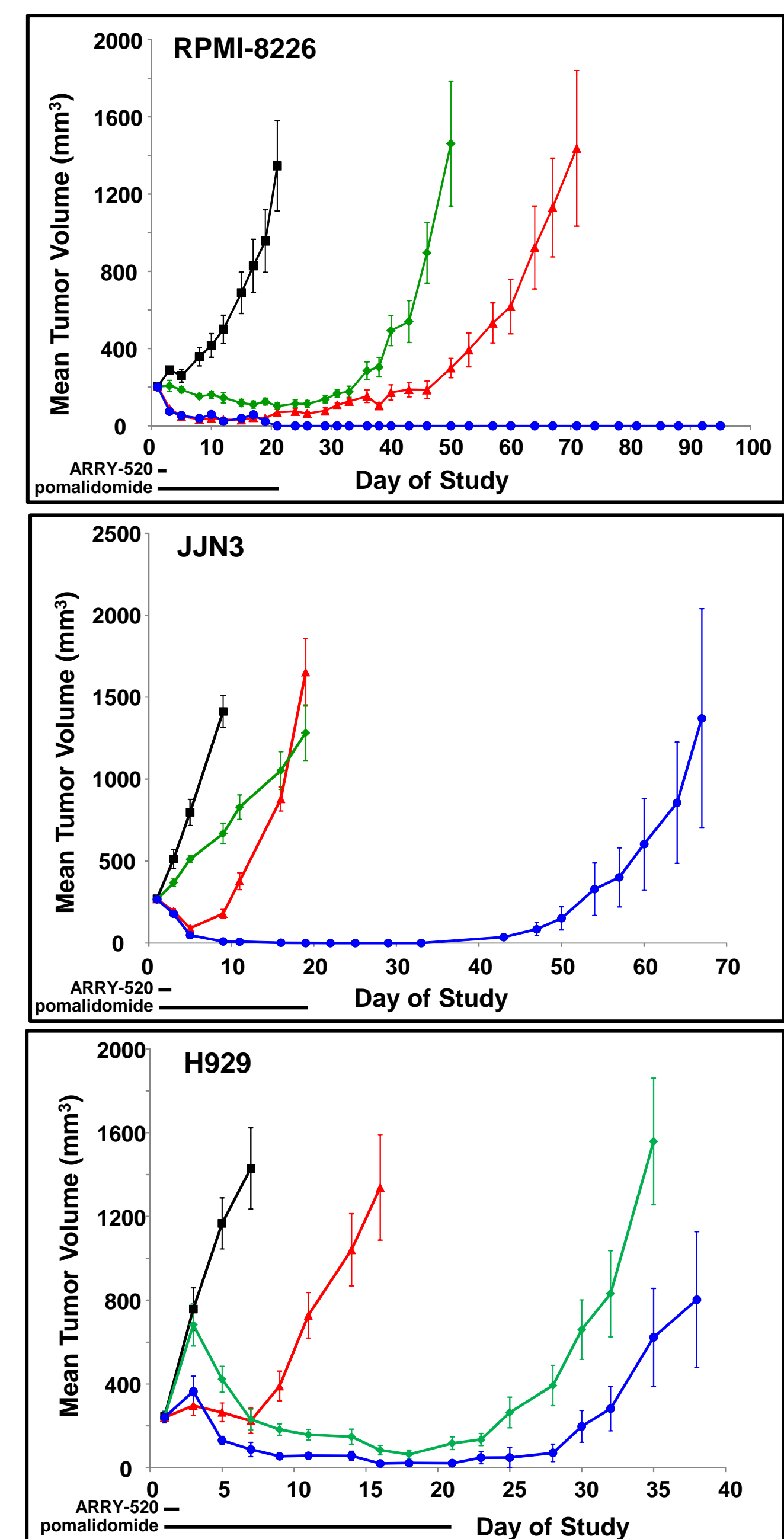
## Co-administration of ARRAY-520 and Pomalidomide does not Impact Exposure



Analyte	C <sub>max</sub> (µg/mL)	AUC <sub>last</sub> (µg*hr/mL)	T <sub>max</sub> (hr)
○ ARRAY-520 (alone)	1.66	3.09	0.083
● ARRAY-520 (combination)	1.76	2.77	0.25
△ pomalidomide (alone)	0.956	3.08	0.083
▲ pomalidomide (combination)	0.997	3.95	0.50

Naive male CD-1 mice were administered a single intraperitoneal (IP) bolus dose of ARRAY-520 (12.5 mg/kg) and/or pomalidomide (10 mg/kg). Plasma concentration of analytes were measured at the indicated time points.

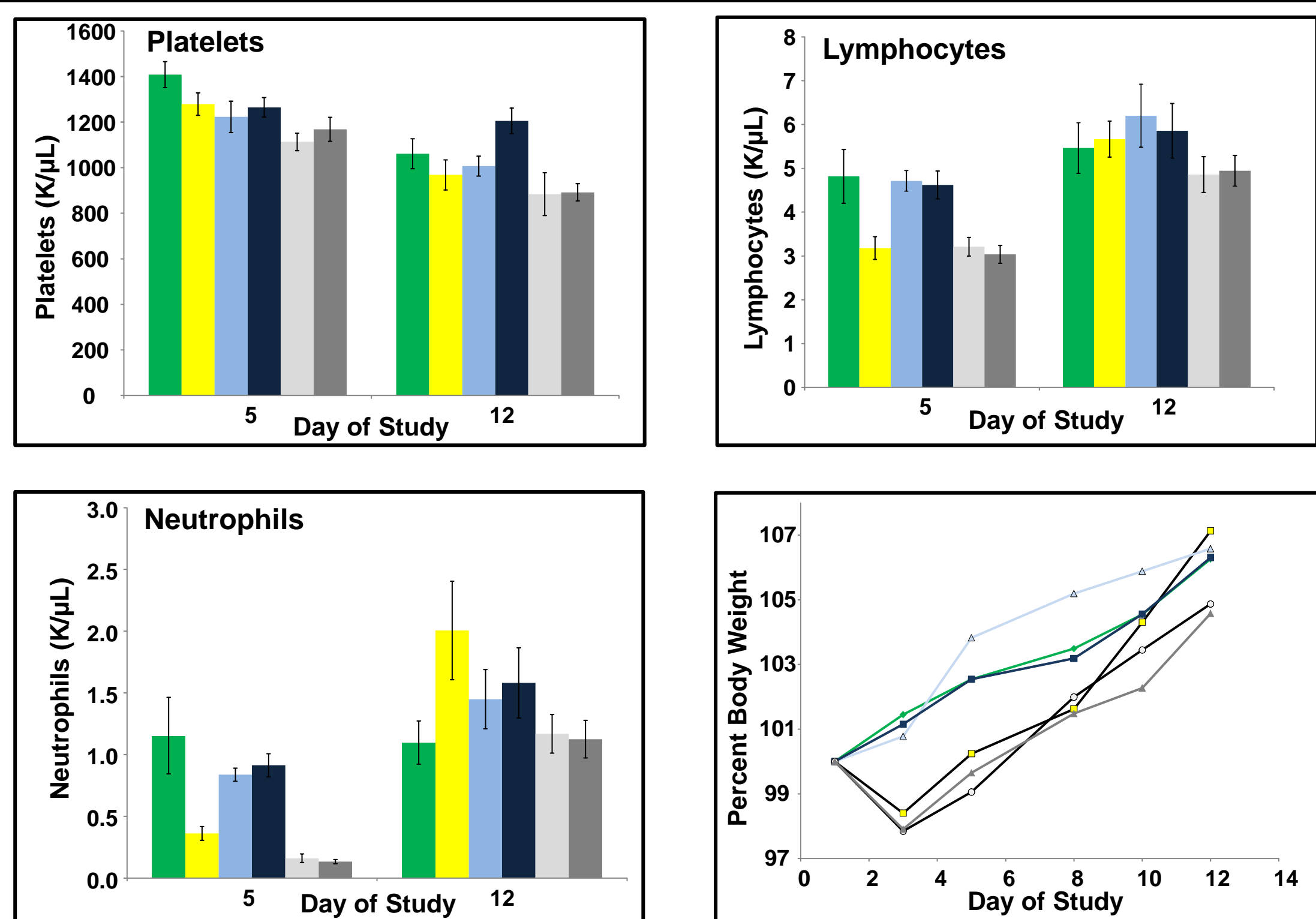
## Co-administration of ARRAY-520 with Pomalidomide Enhances Efficacy



	% Complete Response			% Max Body Weight Loss		
	RPMI-8226	JJN3	H929	RPMI-8226	JJN3	H929
■ vehicle	0	0	0	1.8	1.0	0.8
▲ ARRAY-520	50	0	0	5.3	6.6	8.9
◆ pomalidomide	12.5	0	28.5	0.9	0	4.4
● combination	100	100	57	7.4	7.9	11.6

MM tumor bearing female SCID-Beige mice were administered ARRAY-520 (12.5 mg/kg, Days 1 and 2) and/or pomalidomide (10 mg/kg, QD, Days 1-21 (RPMI-8226 and H929) or Days 1-19 (JJN3)) as an IP bolus dose. Tumor size and animal body weight were measured on the indicated days over the course of each study. % complete response= no palpable tumor for 2 consecutive measurements

## Co-administration of ARRAY-520 and Pomalidomide Shows Acceptable Tolerability



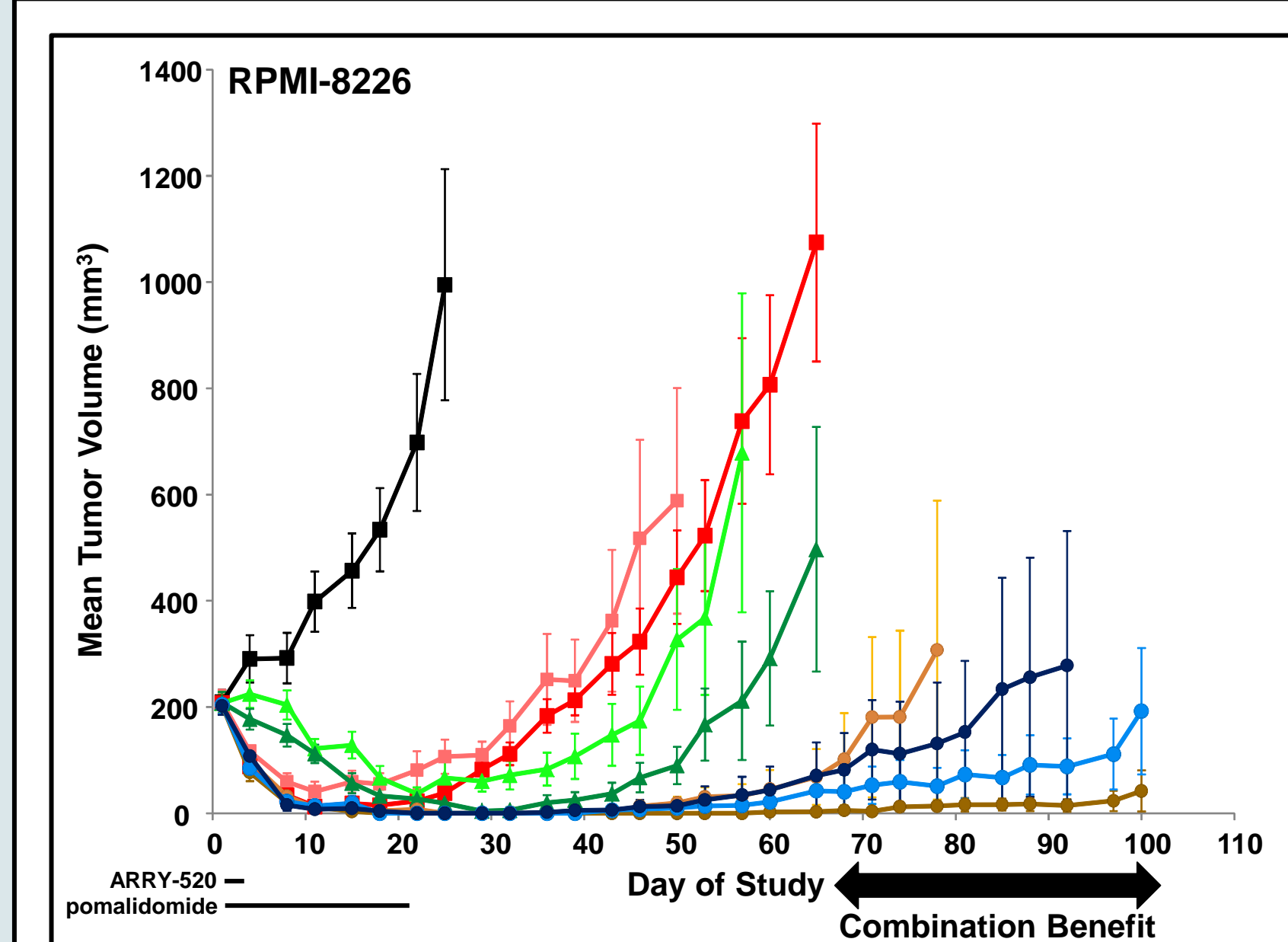
	% Decrease in Cell Counts from Vehicle						% Max Body Weight Loss
	Platelets		Lymphocytes		Neutrophils		
	Day 5	Day 12	Day 5	Day 12	Day 5	Day 12	
◆ vehicle	-	-	-	-	-	-	0
■ 12.5 mg/kg ARRAY-520	9	0	34	0	69	0	0
△ 1 mg/kg pomalidomide	8	0	9	0	27	0	0
■ 10 mg/kg pomalidomide	10	0	4	0	21	0	0
○ 12.5 mg/kg ARRAY-520+ 1 mg/kg pomalidomide	21	17	33	11	86	0	2.2
▲ 12.5 mg/kg ARRAY-520+ 10 mg/kg pomalidomide	17	16	37	10	88	0	2.1

Naive male CD-1 mice were administered ARRAY-520 (12.5 mg/kg, Days 1 and 2) and/or pomalidomide (1, 5, or 10 mg/kg, QD, Days 1-14 as an IP bolus dose). Hematology parameters and animal body weight were measured on the indicated days over the course of the study.

## Summary and Conclusions

- Co-administration of ARRAY-520 with pomalidomide substantially enhanced efficacy
  - Marked increases in complete response rates were observed in two of three MM models
  - Dose reductions of both compounds displayed equivalent combination efficacy
- Co-administration of ARRAY-520 with pomalidomide did not alter exposure
- Co-administration ARRAY-520 with pomalidomide displayed acceptable tolerability
  - No marked decreases in lymphocytes or platelets, body weight loss was minor and acceptable
  - Neutrophils decreases were expected, co-administration moderately enhanced neutrophil loss (day 5) that was rapidly reversible (day 12)
- The novel combination of ARRAY-520 and pomalidomide is a highly active preclinical regimen with acceptable tolerability that warrants further investigation in future clinical trials in patients with MM

## Dose Reductions of ARRAY-520 and/or Pomalidomide do not Impact Combination Efficacy



	% Cure Rate	% Max Body Weight Loss
■ vehicle	0	1.6
■ 7.5 mg/kg ARRAY-520	0	3.7
■ 12.5 mg/kg ARRAY-520	0	8.0
▲ 5 mg/kg pomalidomide	0	0.5
▲ 10 mg/kg pomalidomide	0	1.4
● 7.5 mg/kg ARRAY-520+ 5 mg/kg pomalidomide	62.5	3.4
● 7.5 mg/kg ARRAY-520+ 10 mg/kg pomalidomide	75	6.2
● 12.5 mg/kg ARRAY-520+ 5 mg/kg pomalidomide	50	7.7
● 12.5 mg/kg ARRAY-520+ 10 mg/kg pomalidomide	50	10.2

MM tumor bearing female SCID-Beige mice were administered ARRAY-520 (7.5 or 12.5 mg/kg, Days 1 and 2) and/or pomalidomide (5 or 10 mg/kg, QD, Days 1-21 as an IP bolus dose). Tumor size and animal body weight were measured on the indicated days over the course of the study. % cure rate= no palpable tumor for 158 days from study start

All studies were performed in accordance with IACUC guidelines and in harmony with the Guide for Laboratory Animal Care and Use

