

## Abstract 410

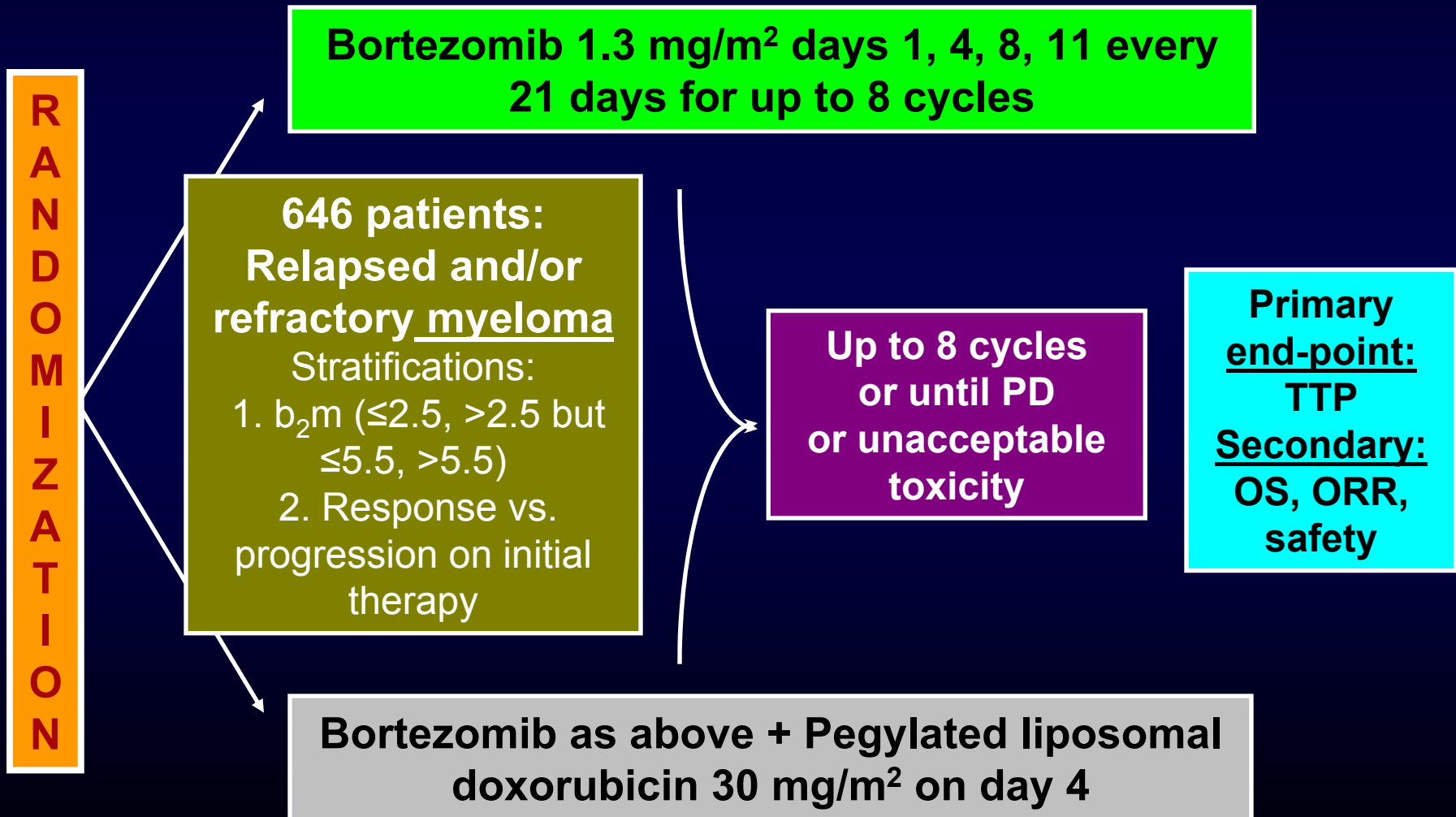
# The Prolonged Time to Progression with Pegylated Liposomal Doxorubicin + Bortezomib Versus Bortezomib Alone in Relapsed or Refractory Multiple Myeloma is Unaffected by Extent of Prior Therapy or Previous Anthracycline Exposure

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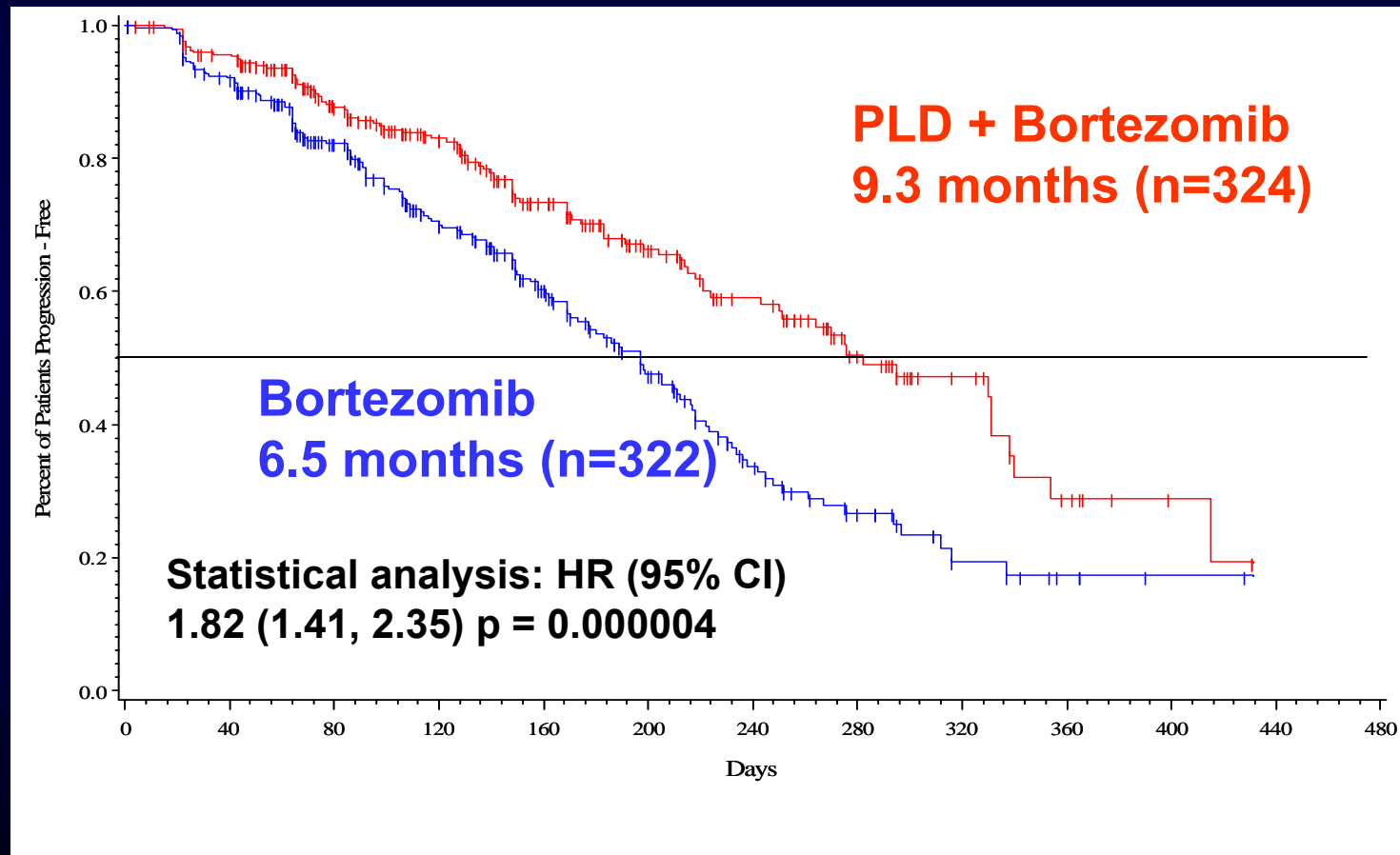
# Disclosures for All Authors

Research Support	Joan Blade, Jesus San Miguel, Arnon Nagler, Pieter Sonneveld, Andrew Spencer, Tadeusz Robak, Jean-Luc Harousseau, & Robert Orłowski have received research funding from J&J
Employee	Kathleen Hennessey, Suneel Mundle & Sen H. Zhuang are employees of J&J
Consultant	Joan Blade, Jesus San Miguel, Pieter Sonneveld
Major Stockholder	Kathleen Hennessey, Suneel Mundle & Sen H. Zhuang are stockholders in J&J
Speakers Bureau	Jesus San Miguel, Andrew Spencer, Jean-Luc Harousseau, Robert Orłowski
Honoraria	Joan Blade, Jesus San Miguel, Pieter Sonneveld, Jean-Luc Harousseau
Scientific Advisory Board	None

# DOXIL-MMY-3001 Study Design



# Time to Progression (MMY 3001-all patients)\*



\* Orłowski R, et al. JCO 2007;. 25:3892-3901

# Rationale for Subgroup Analysis

- Patients exposed to multiple prior therapies are at higher risk of disease progression
- Pre-specified subgroup analysis of this trial was planned to assess:
  - Impact of prior therapies (1 vs.  $\geq 2$ )
  - Influence of previous anthracycline exposure

# MMY 3001

646 patients

1 Prior Therapy  
(219 patients)

≥2 Prior Therapies  
(427 patients)

109 patients  
PLD + B

110 patients  
B

215 patients  
PLD + B

212 patients  
B

# Baseline Characteristics

## (≥ 2 Prior Therapies)

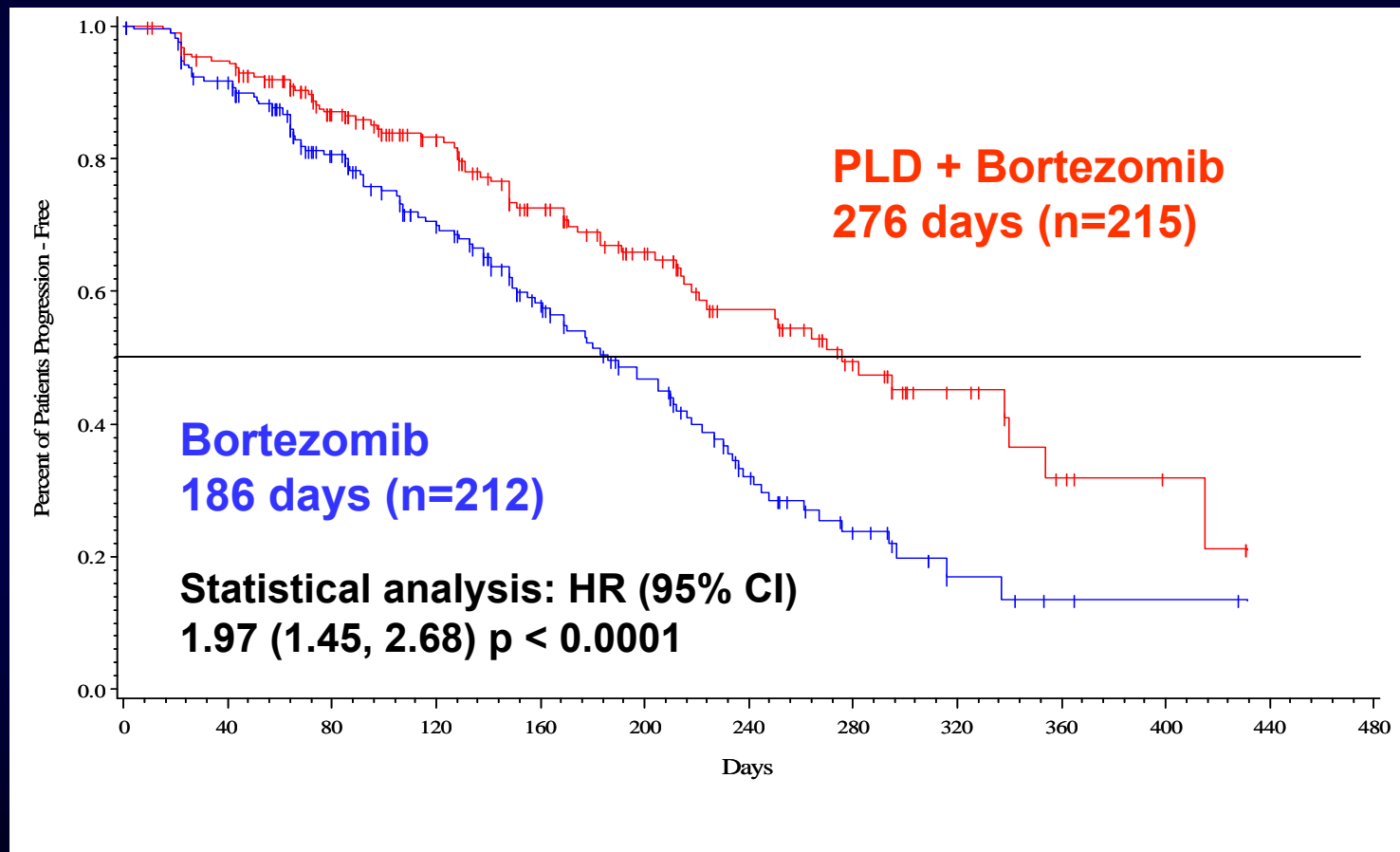
		Bortezomib N=212	PLD + Bortezomib N=215
<b>Median Age (yrs)</b>		61	61
<b>Gender</b>	Male	53%	58%
<b>Race</b>	White	93%	87%
<b>MM Type</b>	IgG, IgA/D/M, L-chain	67%, 23%, 10%	57%, 28%, 13%
<b>Months since initial diagnosis</b>	Median	42.7 mos.	42.1 mos.
<b>β<sub>2</sub>-m (mg/L)</b>	≤2.5	16%	12%
	>2.5 - ≤5.5	53%	57%
	>5.5	32%	31%
<b>Response to initial therapy</b>	Responded, then progressed	94%	94%
	Primary refractory	6%	6%
<b>Cytogenetic abnormality</b>	Yes	17%	16%
	Not done	60%	59%

# Time to Progression (Prior Therapy)

	PLD + Bortezomib (vs. Bortezomib) 1 prior therapy	PLD + Bortezomib (vs. Bortezomib) ≥ 2 prior therapies	Heterogeneity test*
<b>Median Time To Progression</b>	<b>330 days (vs. 199 days)</b>	<b>276 days (vs. 186 days)</b>	
<b>Hazard Ratio (95% CI, log rank p value)</b>	<b>1.71 (1.03, 2.84) log rank p=0.036</b>	<b>1.97 (1.45, 2.68) log rank p&lt;0.0001</b>	<b>p = 0.523</b>

\* Treatment by subgroup (1 prior therapy, ≥ 2 prior therapies) interaction test from the Cox model

# Time to Progression ( $\geq 2$ Prior Therapies)

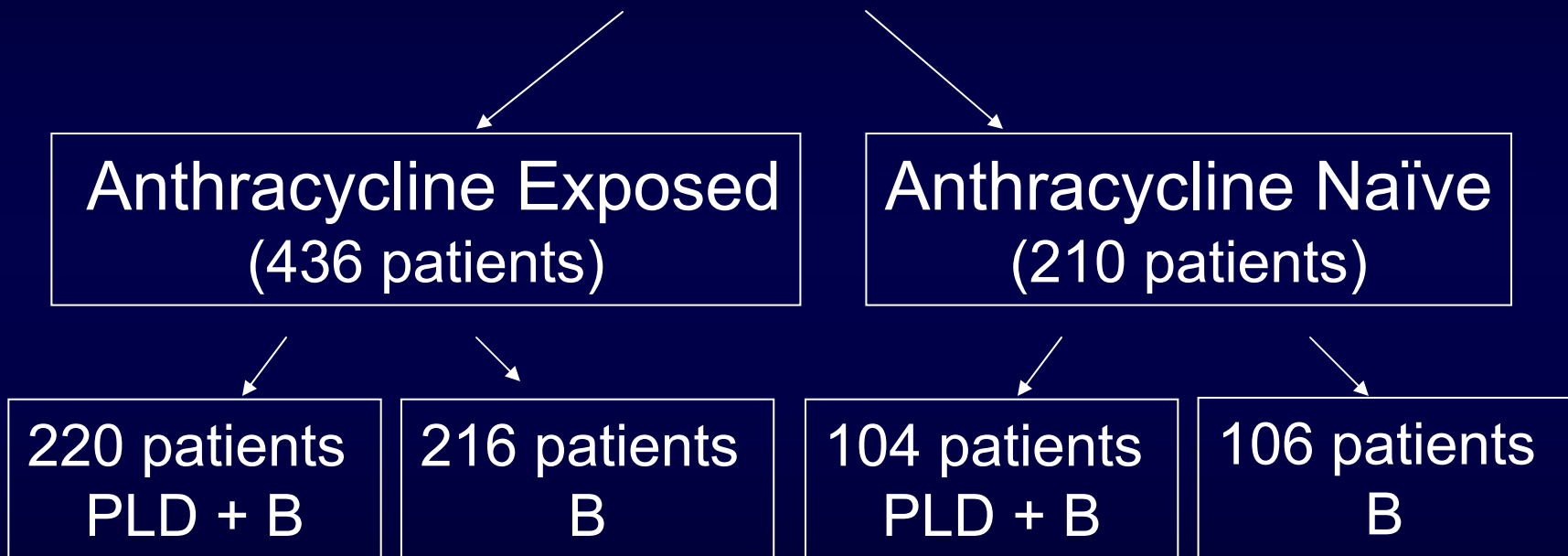


# Adverse Events of Clinical Interest (Prior Therapy)

	PLD + Bortezomib (1 prior therapy, N=107)		PLD + Bortezomib (≥ 2 prior therapies, N=211)	
	Total (%)	Grade 3/4 (%)	Total (%)	Grade 3/4 (%)
Peripheral neuropathy	32	2	36	6
Neutropenia	31	26	36	31
Febrile neutropenia	4	4	3	3
Bleeding/hemorrhage	15	4	14	4
Mucositis/stomatitis	22	3	19	2
Hand foot syndrome	17	4	15	5
Thromboembolic events	2	2	0	0
Alopecia	2	0	1	0
Symptomatic cardiac	6	-	8	-

# MMY 3001

646 patients



# Baseline Characteristics (Anthracycline Exposed)

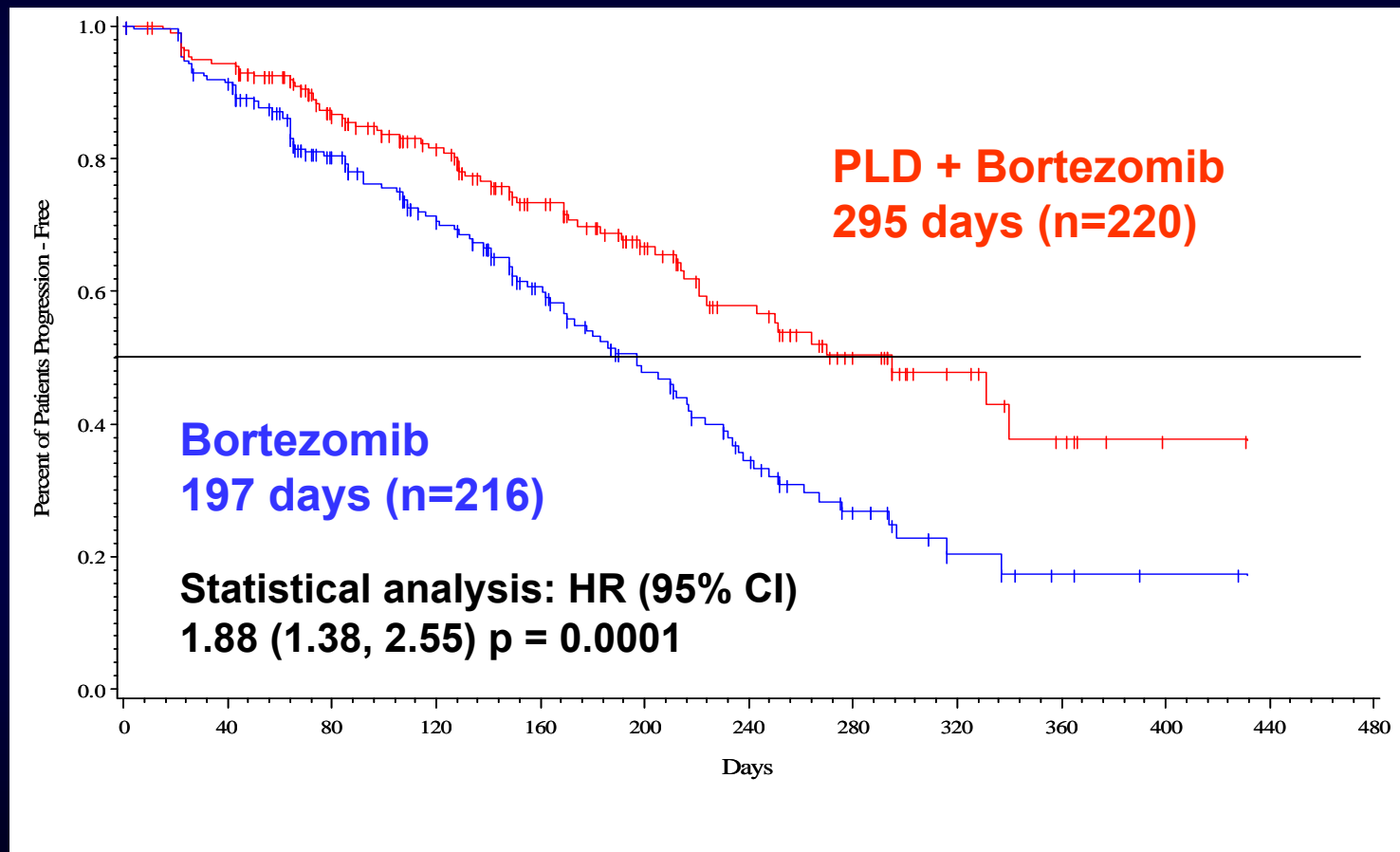
		Bortezomib N=216	PLD + Bortezomib N=220
<b>Median Age (yrs)</b>		59	59
<b>Gender</b>	Male	59%	62%
<b>Race</b>	White	94%	89%
<b>MM Type</b>	IgG, IgA/D/M, L-chain	66%, 22%, 11%	56%, 29%, 14%
<b>Months since initial diagnosis</b>	Median	39.8 mos.	40.8 mos.
<b><math>\beta_2</math>-m (mg/L)</b>	$\leq 2.5$	14%	16%
	$> 2.5 - \leq 5.5$	62%	54%
	$> 5.5$	24%	30%
<b>Response to initial therapy</b>	Responded, then progressed	94%	96%
	Primary refractory	6%	4%
<b>Cytogenetic abnormality</b>	Yes	20%	19%
	Not done	56%	55%
<b>Prior anthracycline</b>	Median total dose (mg/m <sup>2</sup> )	144	144

# Time to Progression (Anthracycline Exposure)

	PLD + Bortezomib (vs. Bortezomib) Anthracycline exposed	PLD + Bortezomib (vs. Bortezomib) Anthracycline naïve	Heterogeneity test*
<b>Median Time To Progression</b>	<b>295 days (vs. 197 days)</b>	<b>282 days (vs. 197 days)</b>	
<b>Hazard Ratio (95% CI, log rank p value)</b>	<b>1.88 (1.38, 2.55) log rank p=0.0001</b>	<b>1.83 (1.12, 2.30) log rank p&lt;.015</b>	<b>p = 0.716</b>

\* Treatment by subgroup (anthracycline exposed , anthracycline naïve) interaction test from the Cox model

# Time to Progression (Anthracycline Exposed)



# Adverse Events of Clinical Interest (Anthracycline Exposure)

	PLD + Bortezomib (Anthracycline exposed, N=215)		PLD + Bortezomib (Anthracycline naive, N=103)	
	Total (%)	Grade 3/4 (%)	Total (%)	Grade 3/4 (%)
Peripheral neuropathy	36	4	33	6
Neutropenia	34	30	35	28
Febrile neutropenia	3	3	4	4
Bleeding/hemorrhage	14	4	14	4
Mucositis/stomatitis	22	2	17	3
Hand foot syndrome	14	6	19	2
Thromboembolic events	1	0	1	1
Alopecia	2	0	0	0
Symptomatic cardiac	8	-	6	-

# Conclusions

- PLD+bortezomib significantly improves TTP compared to bortezomib alone, regardless of the extent of prior therapy or anthracycline exposure
- Safety profile consistent with overall results
- Incidence of SAEs and grade 3 & 4 events consistent across all subgroups
- Low incidence of thromboembolic events

# Acknowledgements

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