

Abstract 8023



AMERICAN SOCIETY OF CLINICAL ONCOLOGY



Impact of prior thalidomide (T) therapy on the efficacy of pegylated liposomal doxorubicin (PLD) and bortezomib (B) in relapsed/refractory multiple myeloma

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Therapeutic consideration for patients with relapsed/refractory multiple myeloma

- Multiple therapeutic options
- Therapeutic goals
 - Optimize TTP and survival
 - Reverse and improve end organ function
 - Minimize treatment-related toxicities
- Factors impacting 2nd line treatment choice
 - **Response and tolerability to prior therapy**
 - Patient comorbidities
 - Oral vs IV

Rationale for sub group analyses

- Report of possible resistance to lenalidomide in patients previously treated with thalidomide¹
- Pre-specified subgroup analyses of previously reported study (MMY 3001: Bortezomib vs. PLD + Bortezomib) to assess:
 - The difference in efficacy (TTP, OS, response rates) between treatment groups in patients with prior exposure to thalidomide/lenalidomide (IMiD) therapy
 - Whether efficacy differs based upon prior exposure to IMiD therapy

DOXIL-MMY-3001 Study Design

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Bortezomib 1.3 mg/m² days 1, 4, 8, 11 every 21 days for up to 8 cycles

646 patients:
Relapsed and/or refractory myeloma

Stratifications:

1. β_2m (≤ 2.5 , > 2.5 but ≤ 5.5 , > 5.5)
2. Response vs. progression on initial therapy

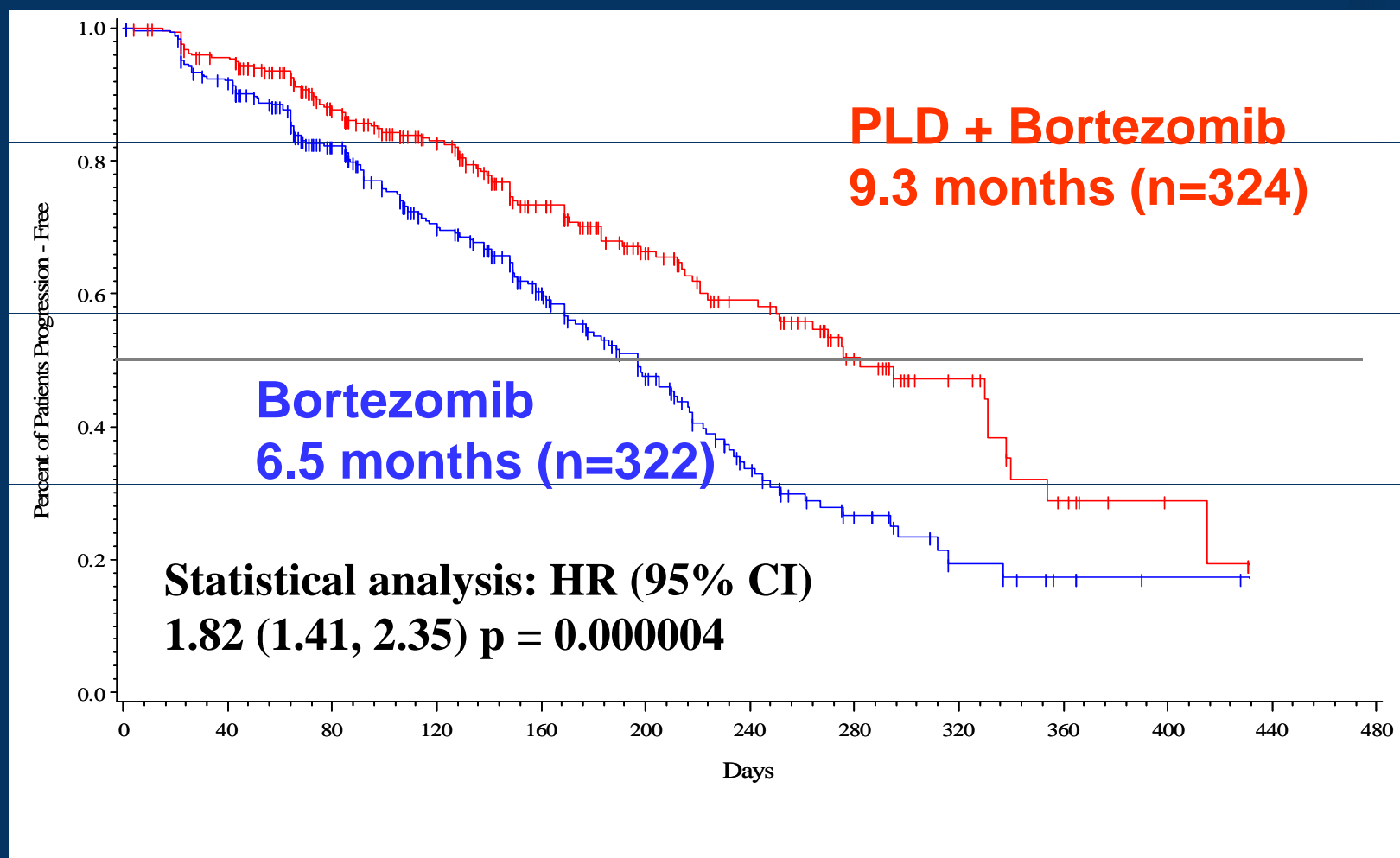
Up to 8 cycles or until PD or unacceptable toxicity

Primary endpoint:
TTP

Secondary:
OS, ORR, safety

Bortezomib as above + Pegylated liposomal doxorubicin 30 mg/m² on day 4

Time to Progression (MMY 3001-all patients)*



MMY 3001

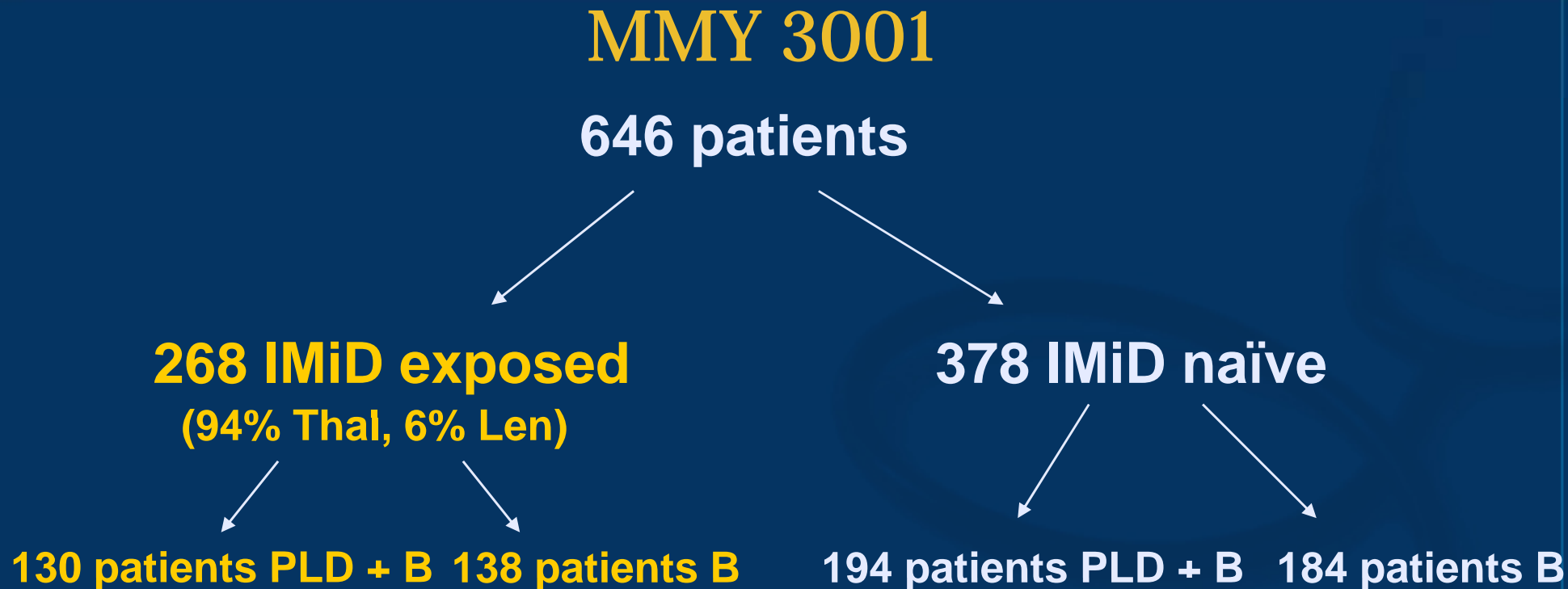
646 patients

268 IMiD exposed
(94% Thal, 6% Len)

378 IMiD naïve

130 patients PLD + B **138 patients B**

194 patients PLD + B **184 patients B**



Baseline Characteristics (IMiD Exposed)

		PLD + Bortezomib N=130	Bortezomib N=138
Mean Age (yrs)		60.7	62.1
Gender	Male	58%	57%
Months since initial diagnosis	Median	46.3 mos.	46.7 mos.
Time since first progression	Median	1.4 mos.	1.6 mos
Albumin (g/dL)		3.75	3.70
β ₂ -microglobulin (mg/L)	≤2.5	17%	17%
	>2.5 - ≤5.5	48%	52%
	>5.5	35%	31%
Cytogenetic abnormality	Not Done	52%	52%
	Yes	19%	19%
	No	28%	28%
	Not Evaluable	2%	1%

Baseline Characteristics (IMiD Exposed)

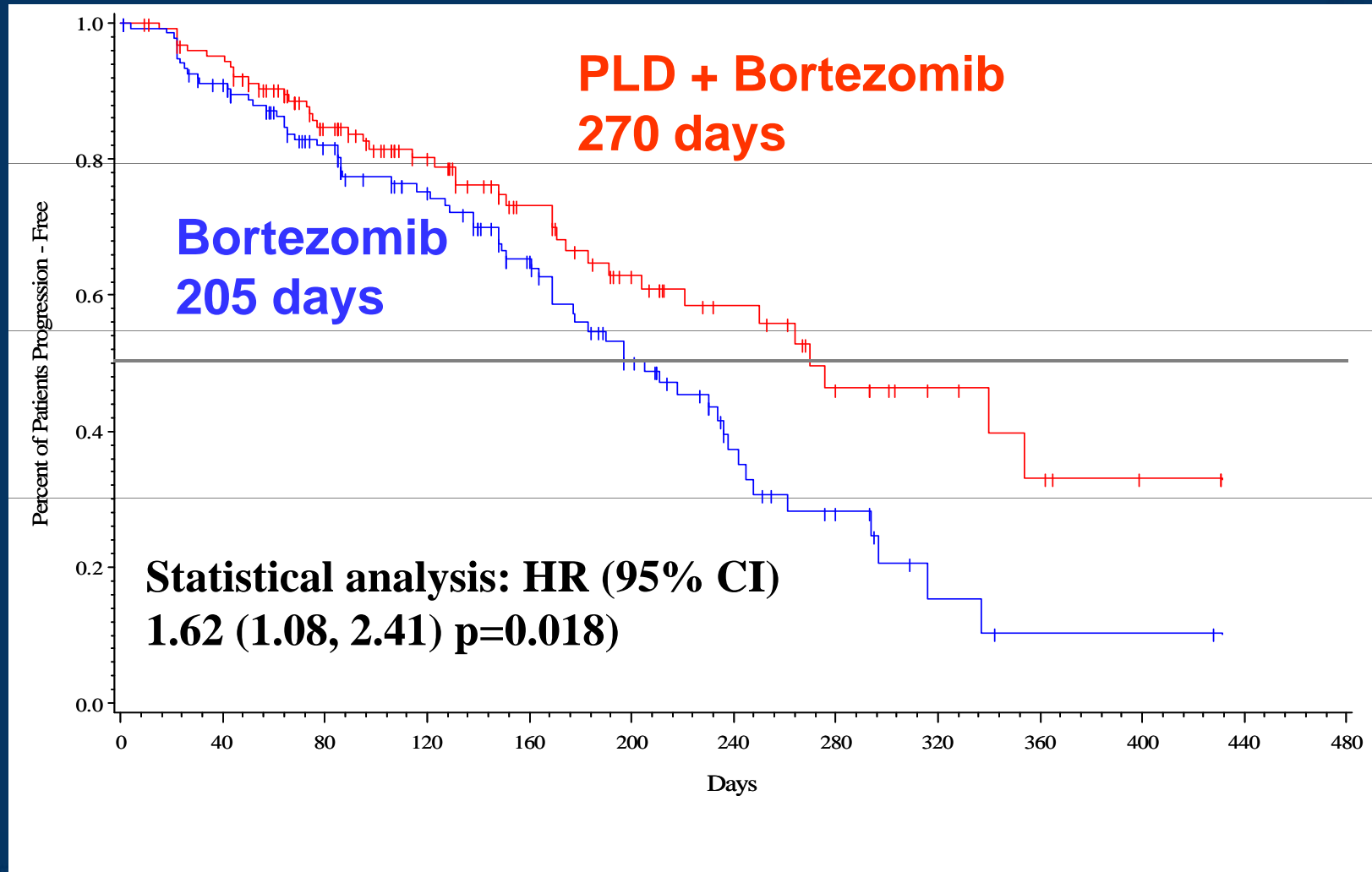
		PLD + Bortezomib N=130	Bortezomib N=138
ECOG Score	0	43%	45%
	1	57%	55%
Number of Prior Therapies	1	8%	12%
	≥2	92%	88%
Type of prior therapy	Corticosteroid	100%	100%
	Alkylating agent	90%	86%
	Anthracycline	79%	70%
	SCT	72%	58%

Time to progression

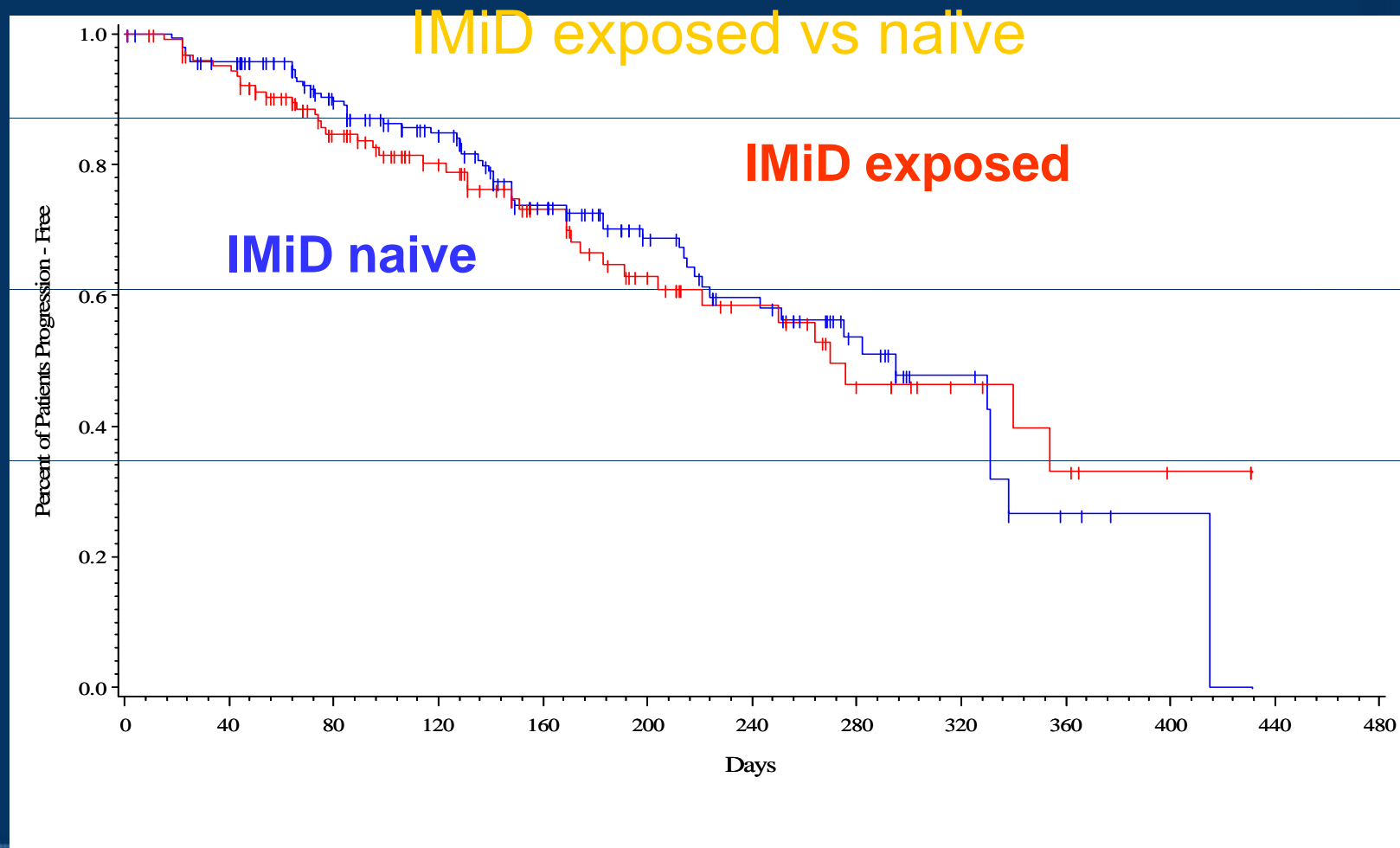
	PLD + Bortezomib (vs. Bortezomib) IMiD exposed	PLD + Bortezomib (vs. Bortezomib) IMiD naive	Heterogeneity test*
Median Time To Progression	270 days (vs 205 days)	295 days (vs 189 days)	
Hazard Ratio (95% CI, log rank p value)	1.62 (1.08, 2.41) log rank p=0.018	2.01 (1.42, 2.84) log rank p<.0001	P = 0.446

*Treatment by subgroup (IMiD exposed, IMiD Naïve) interaction test from the Cox model

Time To Progression (IMiD exposed)



Time to progression (PLD + Bortezomib)



Response Rates

	PLD + Bortezomib (IMiD exposed, N=123)	PLD + Bortezomib (IMiD naive, N=180)
OR (CR+PR)	48%	47%
CR	4%	5%
PR	44%	42%
nCR	9%	9%
CR+VGPR*	31%	27%
Duration of Response (CR+PR)	319 days	310 days

* According to the IMWG criteria

Adverse Events of Clinical Interest

	PLD + Bortezomib (IMiD exposed, N=126)		PLD + Bortezomib (IMiD naive, N=192)	
	Total(%)	Grade 3/4 (%)	Total(%)	Grade 3/4 (%)
Peripheral Neuropathy	40	5	32	4
Neutropenia	33	28	35	31
Febrile Neutropenia	3	3	3	3
Bleeding/hemorrhage	12	3	16	5
Mucositis/stomatitis	21	3	20	2
Hand foot syndrome	17	6	15	4
Thromboembolic Events	0	0	2	1
Alopecia	2	0	1	0
Symptomatic Cardiac	8	-	7	-

Comparative Results Based on Prior IMiD Exposure

	PLD + Bortezomib (IMiD exposed, N=130)	Lenalidomide + Dex ^{1,2} (Thal exposed, N=126)
EFFICACY		
Median TTP (days)	270	258 (36.9 weeks)
OR (%)	48	54
CR/nCR (%)	13	11.9
SAFETY (%)	(n=126)	(n=126)
PE + DVT	0	14
Neutropenia (\geq Gr. 3)	28	33
Neuropathy (\geq Gr. 3)	5	4

¹Wang, et al. *BLOOD* 2006. 108(11): p1014a - abstract 3553; ²Wang, et al. *JCO* 2006 ASCO Annual Meeting Proceedings Part I. Vol 24, No. 18S (June 20 Supplement) – Oral presentation based on abstract 7522

Conclusions

- In patients previously exposed to IMiD therapy, TTP is significantly longer with PLD + B compared to bortezomib alone
- TTP in patients treated with PLD + B is comparable between patients who rec'd prior IMiD therapy to those who did not
- Objective response rates, including the rate of CR, and duration of response were comparable between patients treated with PLD + B regardless of whether or not they rec'd prior IMiD therapy

Conclusions (cont.)

- Proportion of patients experiencing adverse events is comparable between those previously exposed to IMiD therapy and those who were not
- Low incidence of thrombovascular events (across all sub groups) which is favorable compared to other second line therapies (e.g., Lenalidomide + Dex)

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Backup slides

Overall Survival (IMiD exposed)

