

SWOG Protocol S0232: Dex +/- Lenalidomide for Previously Untreated Myeloma

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**Southwest
Oncology Group**
A National Clinical Research Group

Disclosures for J. Zonder, MD

In compliance with ACCME policy, ASH requires the following disclosures to the session audience:

Research Support/P.I.	Celgene, Millennium, Cephalon
Employee	No relevant conflicts of interest to declare
Consultant	No relevant conflicts of interest to declare
Major Stockholder	No relevant conflicts of interest to declare
Speaker Engagements	Celgene, Millennium
Honoraria	No relevant conflicts of interest to declare
Scientific Advisory Board	No relevant conflicts of interest to declare

Presentation includes discussion of the following off-label use of lenalidomide and bortezomib (initial treatment of multiple myeloma)

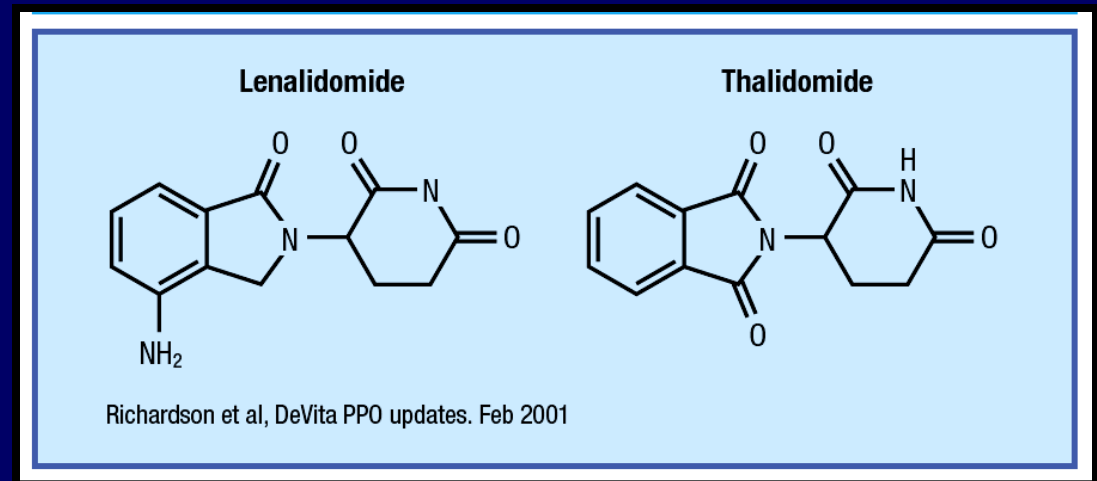
Background: Initial Therapy

- **No “Standard Therapy” exists for NDMM**
 - MP
 - VAD (DVd)
 - **Thal-Dex**
 - Pulse Dex
- **Small minority achieve CR, none cured**
 - ASCT improves CR rate, possibly survival

Background: Initial Therapy

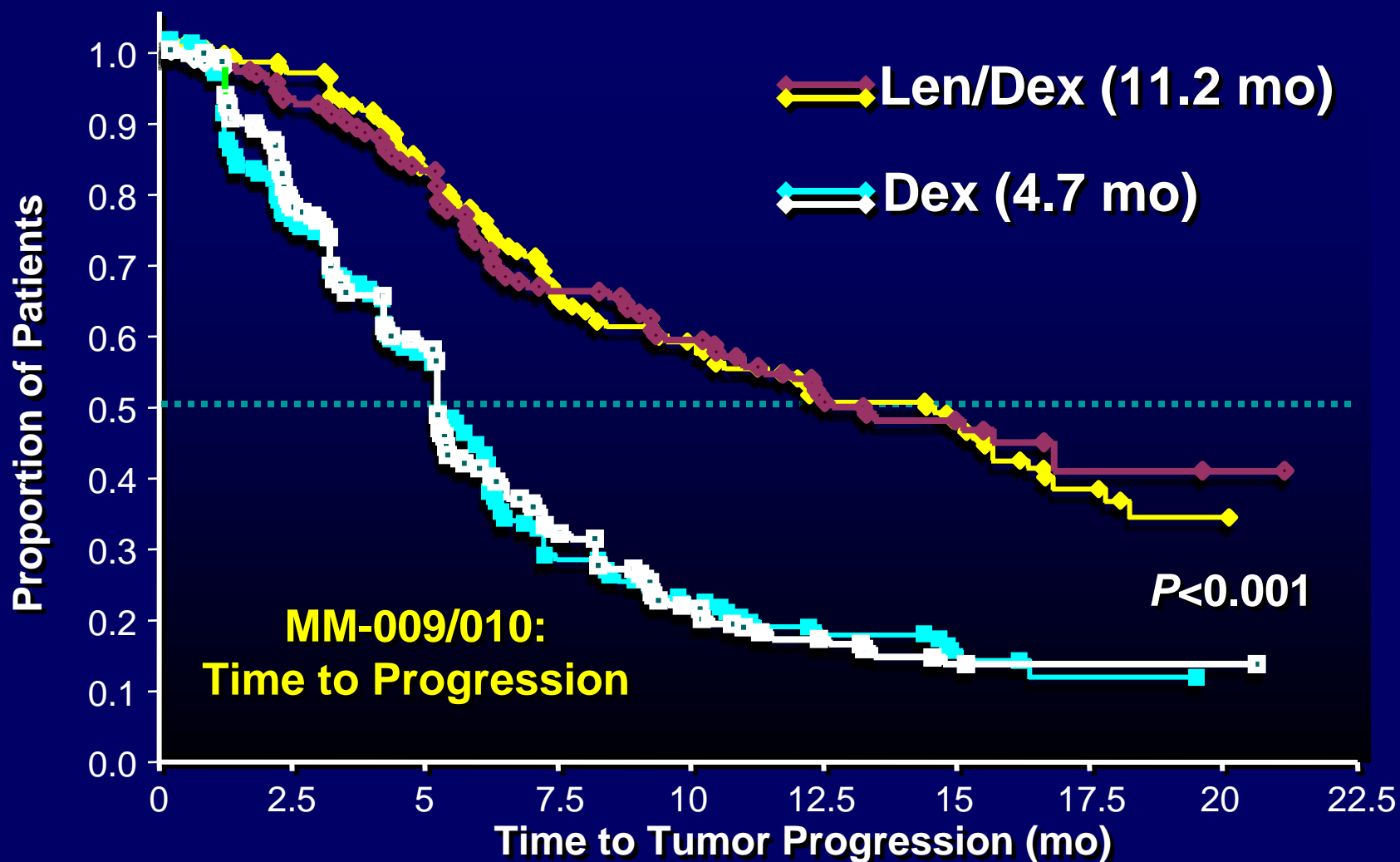
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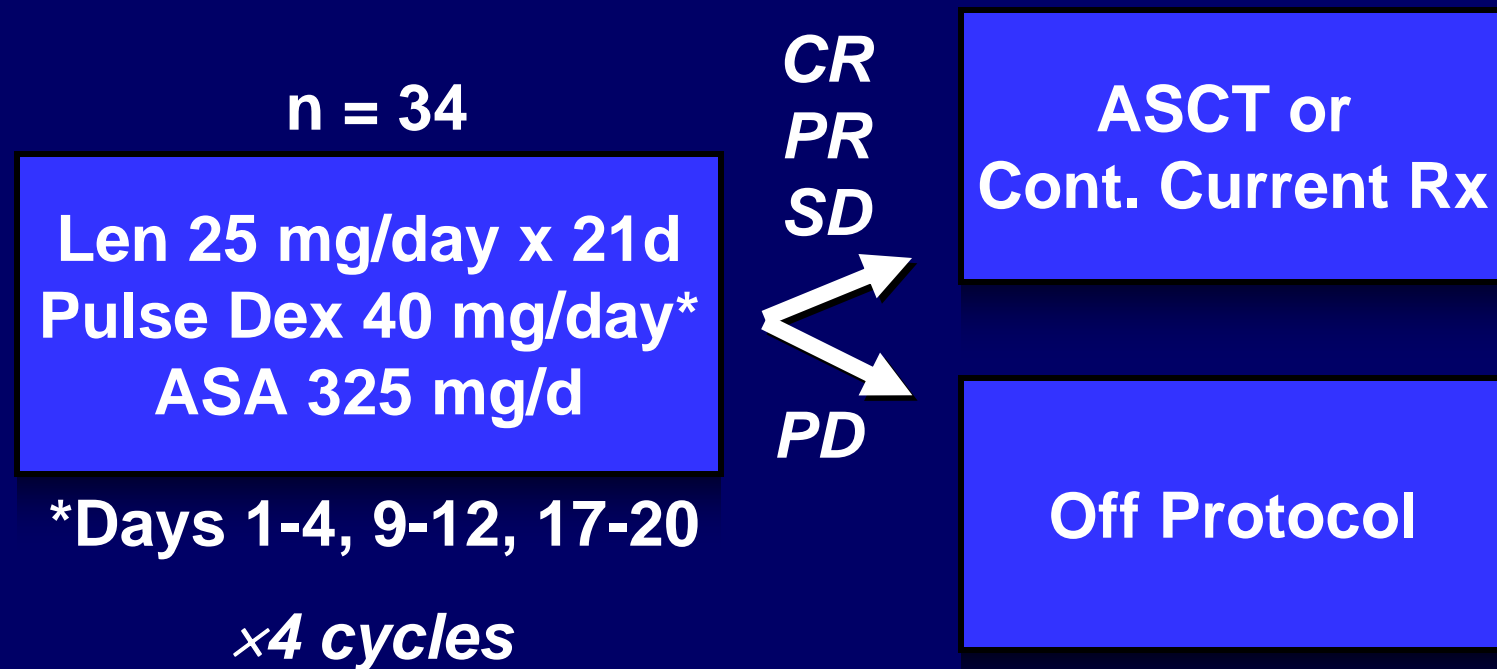
Current goal: Increase CR/nCR while minimizing therapy-related toxicity

Background: Len-Dex in RRMM



Weber D, et al. N Engl J Med 2007;357(21):2133
Dimopoulos M, et al. N Engl J Med 2007;357(21):2123

Background: Phase II Len-Dex vs NDMM

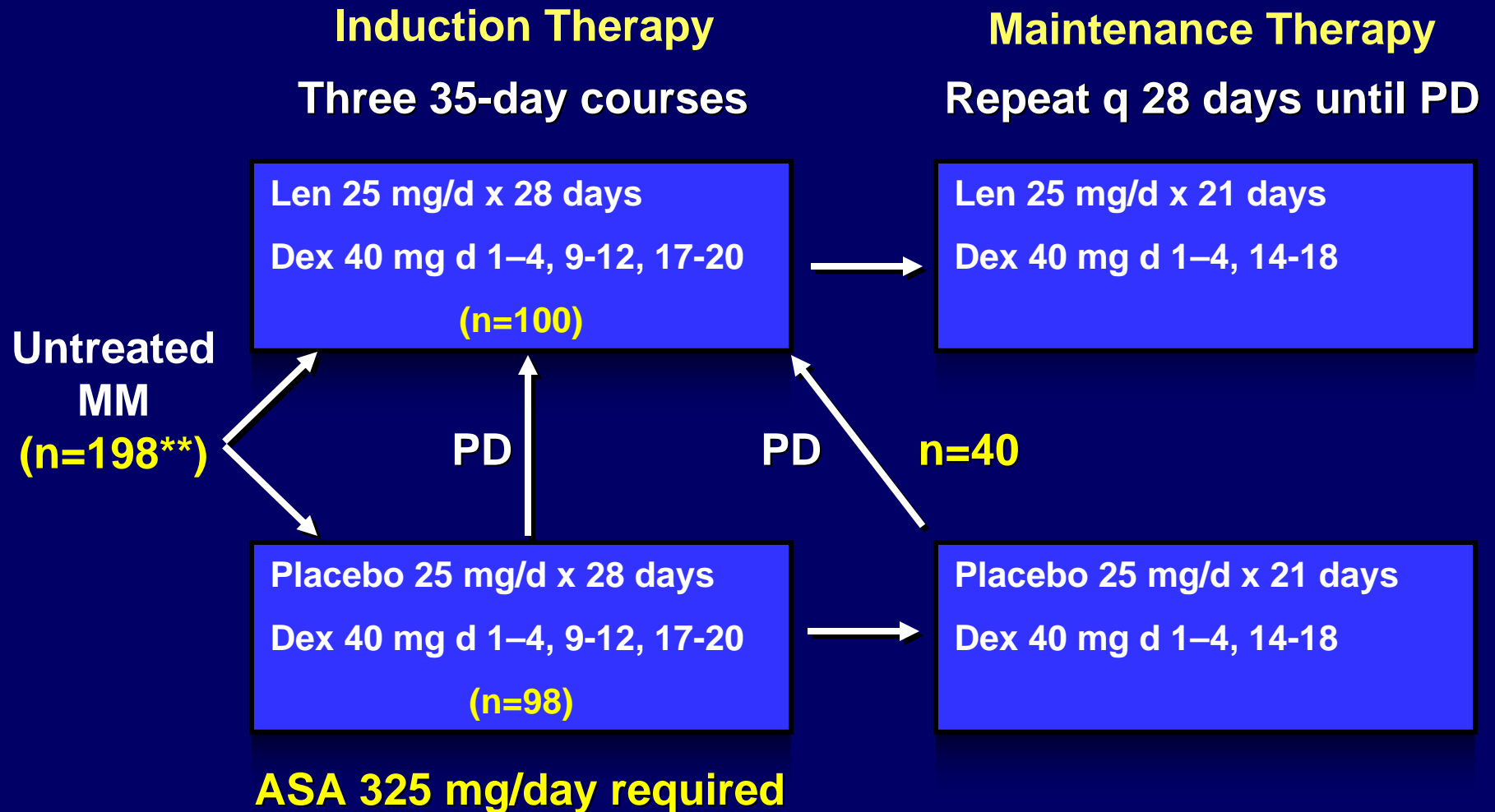


$\geq n$ CR/VGPR: 38% (ORR: 91%)

Rajkumar SV, et al. *Blood*. 2005;106:4050

Lacy MQ, et al. *Mayo Clin Proc*. 2007;82:1179

SWOG S0232: Study Design



****Protocol closed after early interim analysis by DSMC.**

Eligibility

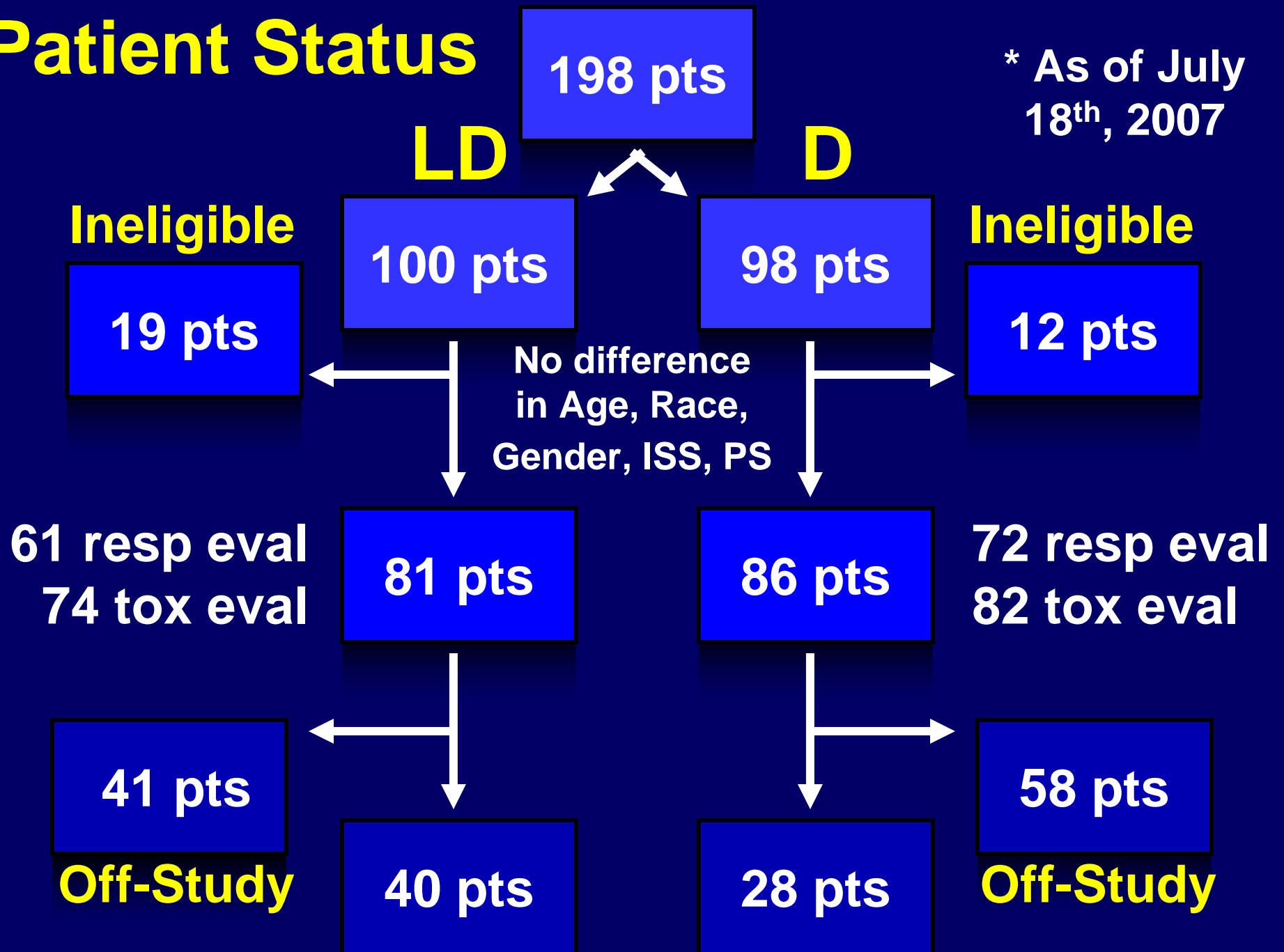
- Ineligible for/declining immediate ASCT
- No prior therapy (≤ 4 d dex allowed)
- Adequate renal, hepatic function
- Measurable disease
 - Serum M-Protein >1000 mg/dL
 - Urine light chain >500 mg/24 hr
- Age ≥ 18 yrs
- Performance Status 0-2 (3 if due to MM)

Stratification

- PS 0-1 vs 2-3
- ISS stage I vs II vs III

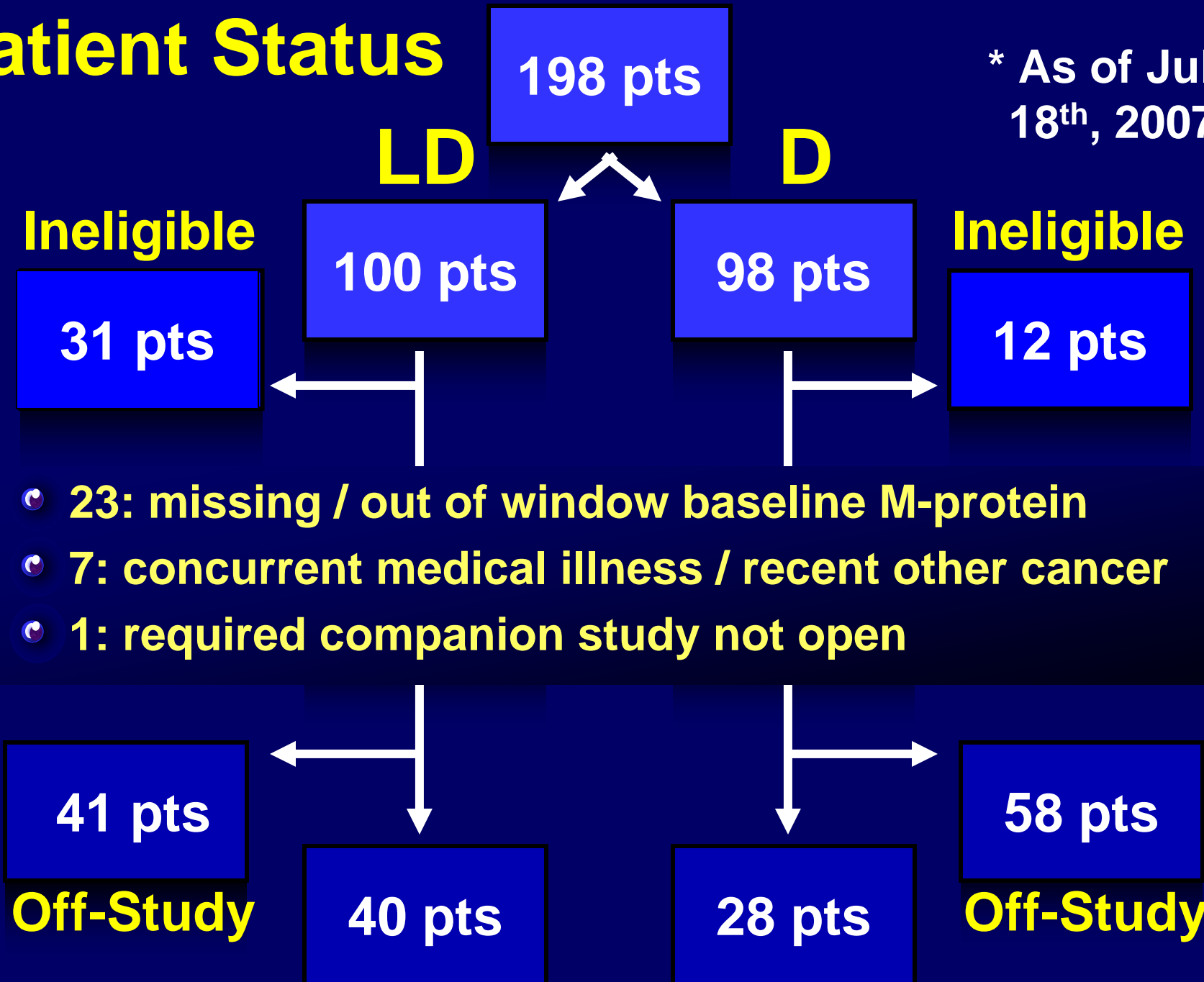
Patient Status

* As of July 18th, 2007



Patient Status

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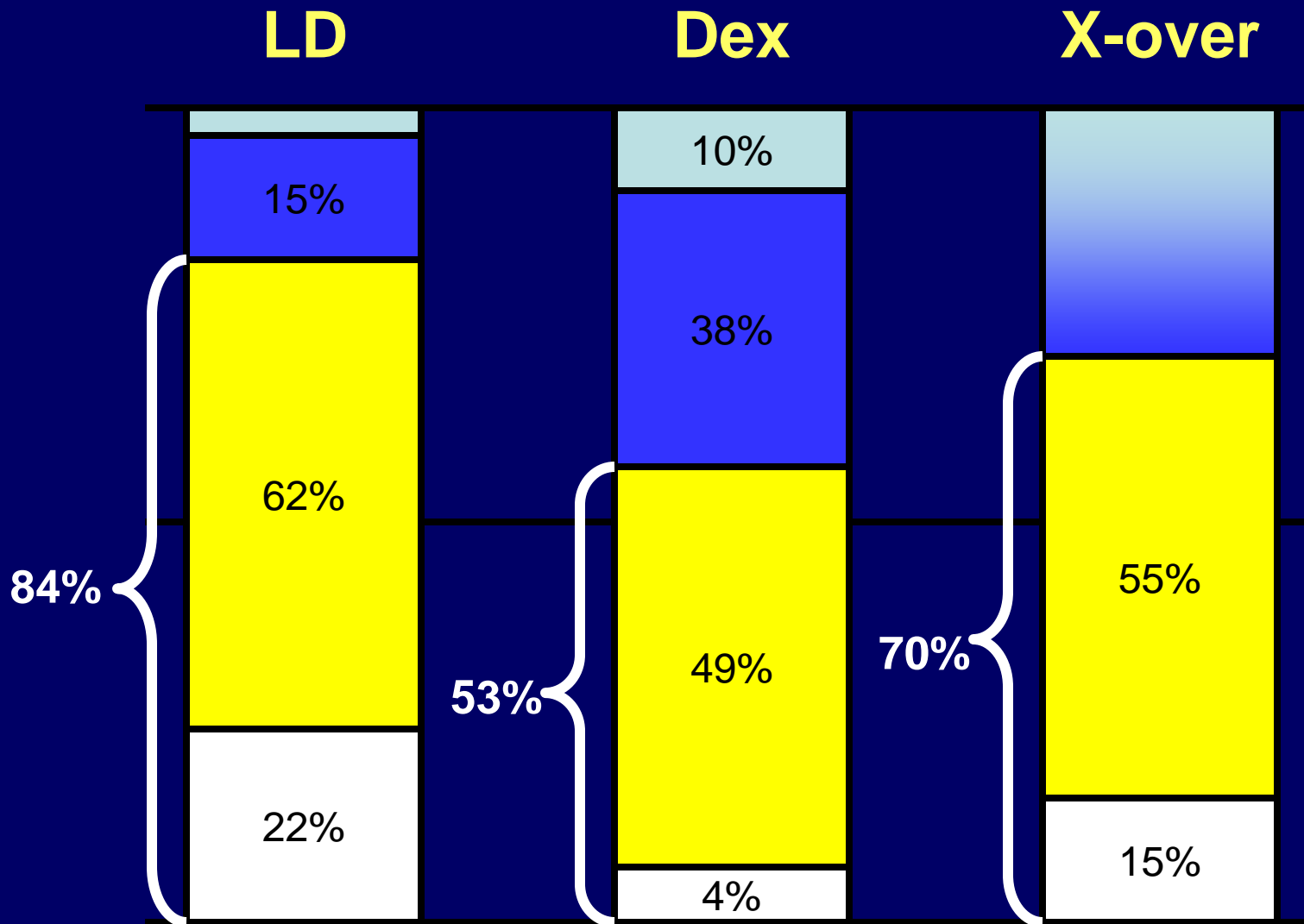
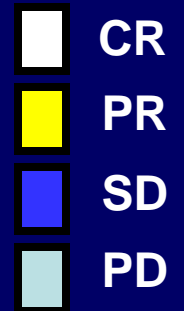


• 23: missing / out of window baseline M-protein

6 • 7: concurrent medical illness / recent other cancer

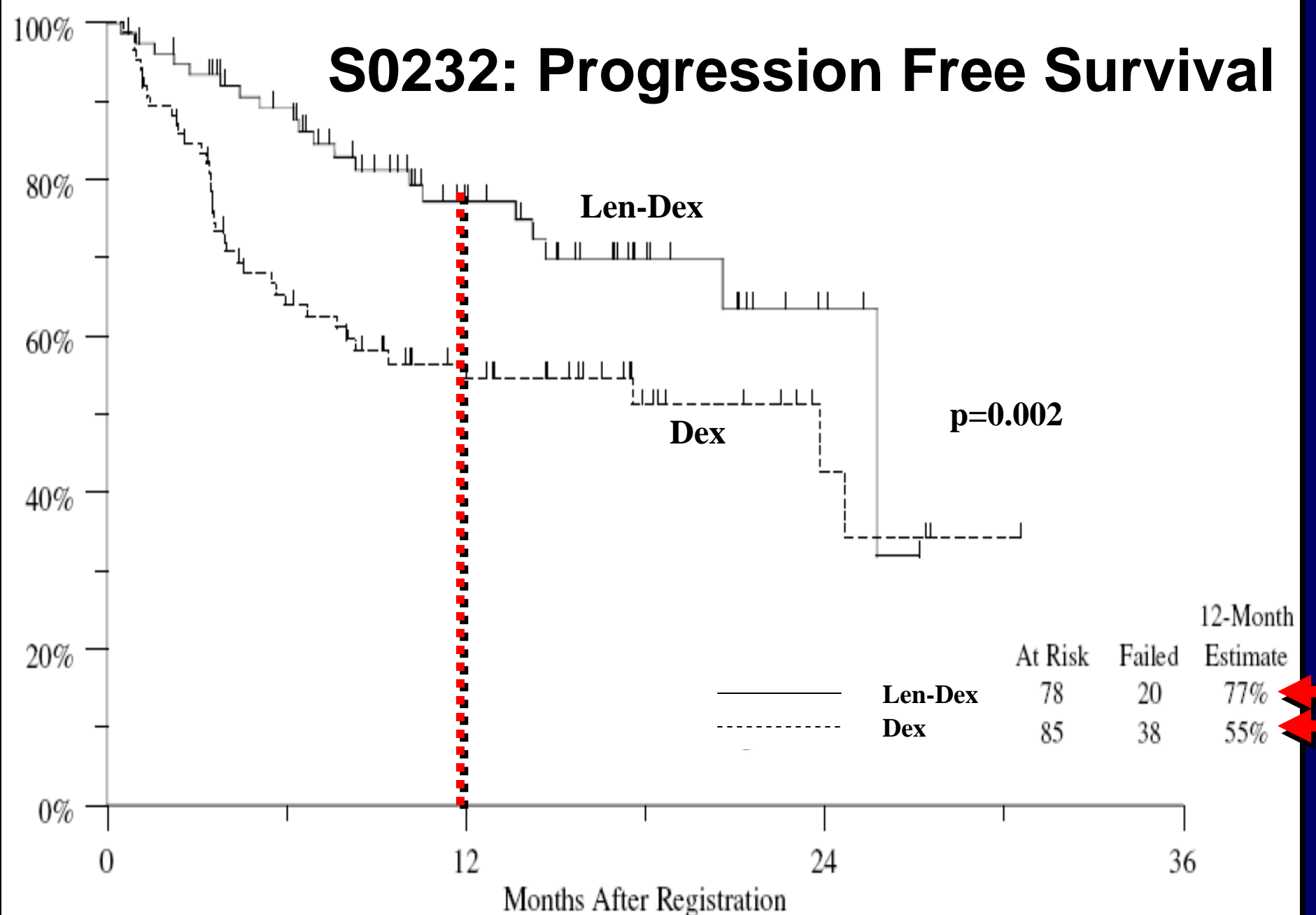
• 1: required companion study not open

Response to Therapy

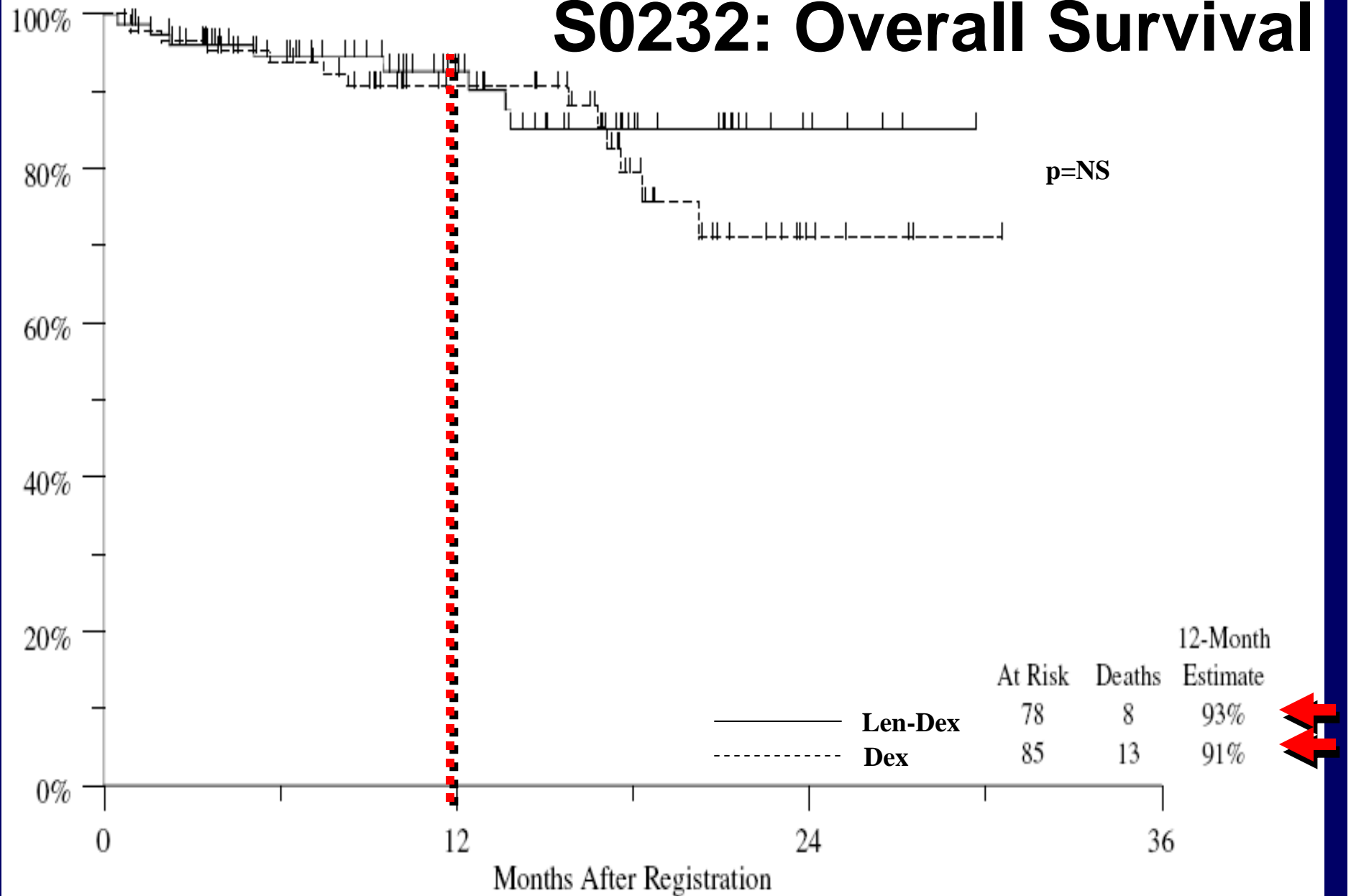


p = 0.001

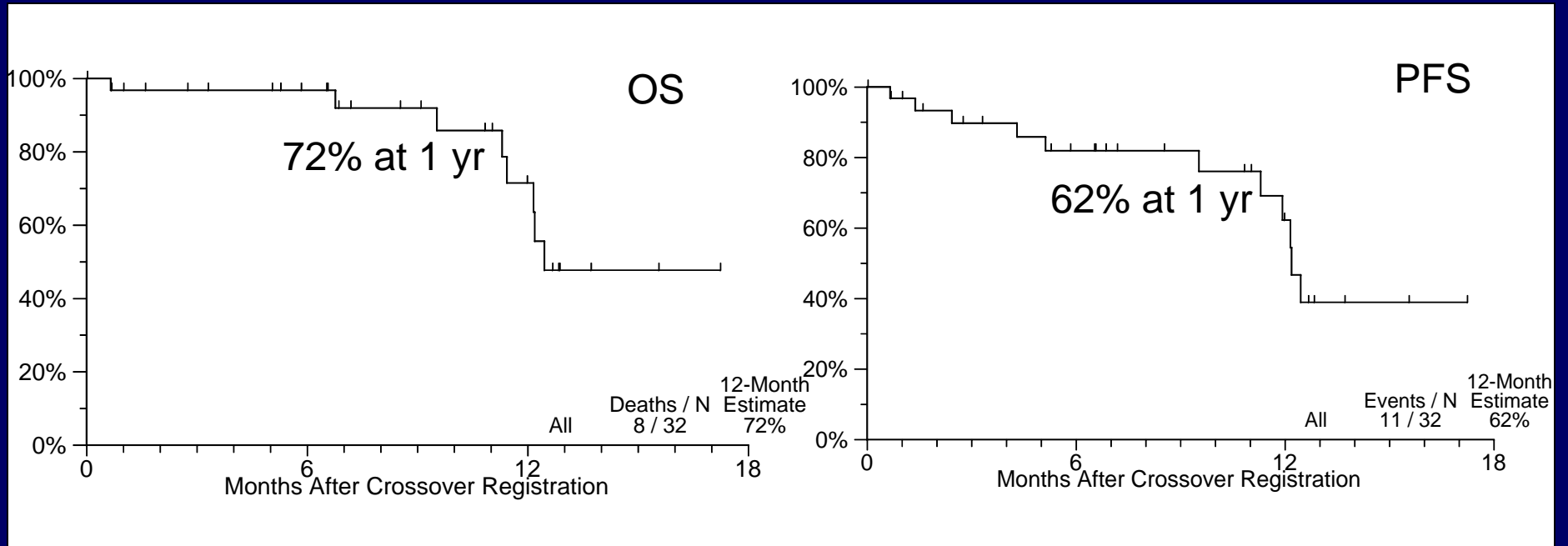
S0232: Progression Free Survival



S0232: Overall Survival



Outcomes after Cross-over to LD



Major Adverse Events

	LD (%)	Dex (%)
Gr.3-4 PLTs	4.2	2.4
Gr.3-4 ANC	13.8	2.4 $p=0.010$
Gr.3-4 Hgb	8.3	9.8
Infections (all)	51.4	28 $p=0.003$
Infections (Gr.3-5)*	18.9	9.8
Hyperglycemia (any)	51.4	57.3
Depression (any)	33.3	20.7

*One participant on LD arm had a Grade 5 (lethal) infection

Thrombotic Events

	LD	Dex	
TEEs	25	7	p = 0.089
no ASA	6	0	
on ASA	14	12	
After X-over		5	

Summary and Discussion

- **LD much more active than Dex vs NDMM**
 - Higher ORR and CR
 - High 1-yr OS rate both arms (↑ with ↓Dex?)
 - Effective salvage with cross-over
- **Toxicity is manageable but not trivial**
 - Grade 3-4 neutropenia ↑, but not PLTs, Hgb
 - Non-neutropenic Infections more common
- **Thrombosis rates remained high on ASA**
 - ASA compliance, other risk factors not known
 - Decreased Dex dose may ↓ clot incidence
 - Optimal prophylaxis not known (?LMWH)

Acknowledgements

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 - Charles Schiffer, MD
 - Multiple Myeloma Research Team
- **Participating Investigators and Patients**