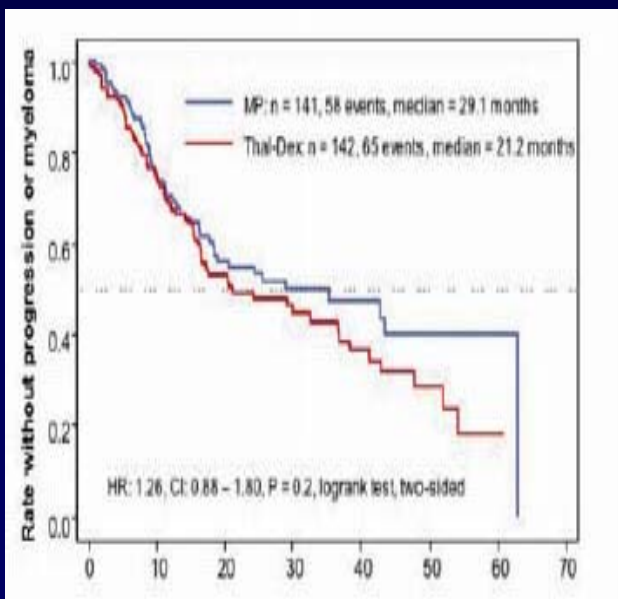


Newly Diagnosed Multiple Myeloma: How Should We Manage the Nontransplant Candidate?

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Division of Hematology
University of Torino
Torino, Italy

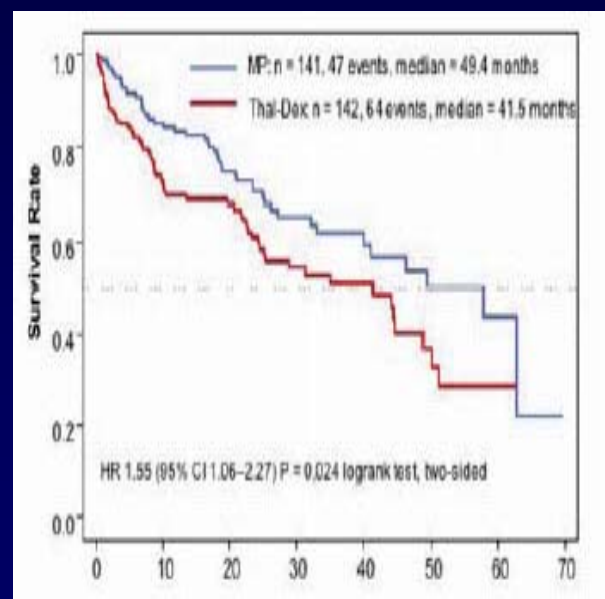
Thal/Dex vs MP in Newly Diagnosed MM

Time to Progression



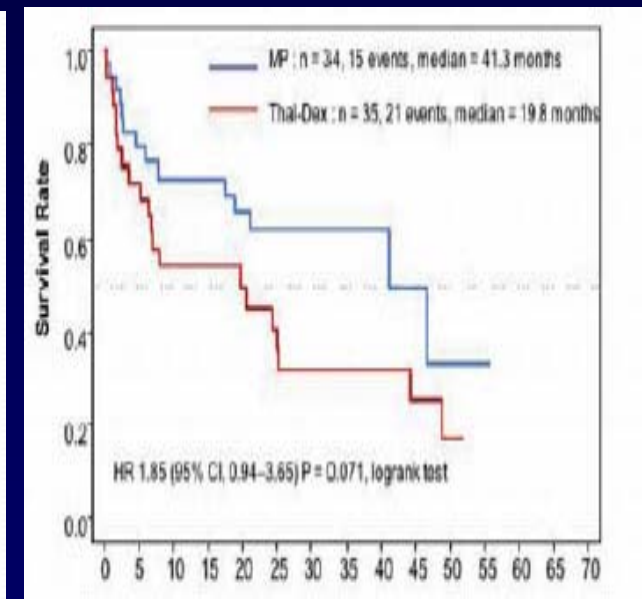
Months

Overall Survival



Months

Survival: Pts >75 Years



Months

MPT: The Current Standard of Care in Elderly Patients

MP-Thal vs MP Studies

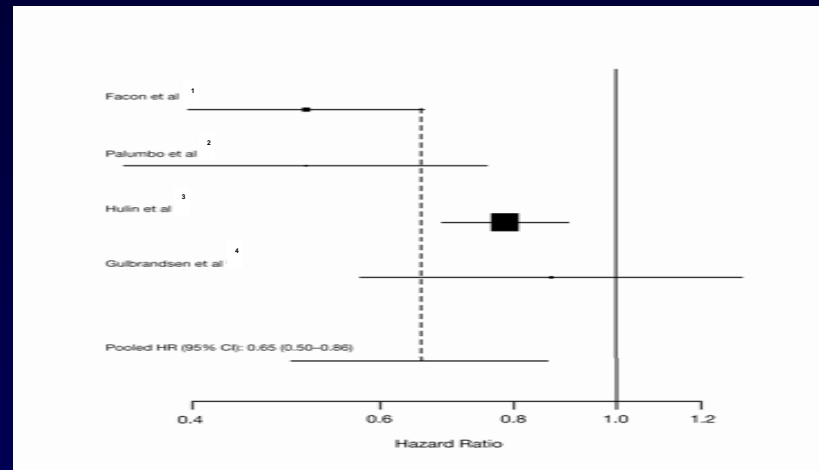
	Median PFS, Months	PFS P Value	Median OS, Months	OS, P Value
IFM¹	27.5 vs 17.8	<.0001	51.6 vs 33.2	.0006
GIMEMA²	N/A	.0006	N/A	NS
IFM³	24.1 vs 19	.001	45.3 vs 27.7	.03
Nordic⁴	16 vs 14	NS	29 vs 33	NS
Hovon⁵	N/A	<.001	N/A	NS

N/A= not available; N.S.= not significant

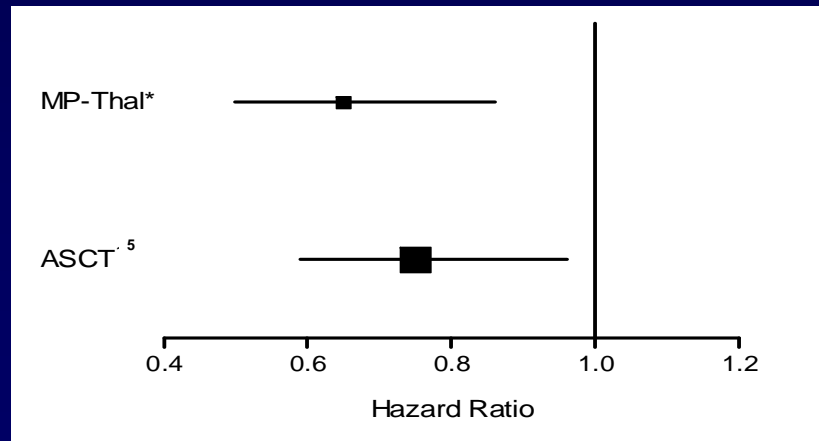
1. Facon T, et al. *Lancet*. 2007;370(9594):1209-1218. 2. Palumbo A, et al. *Lancet*. 2006;367(9513):825-831. 3. Hulin C, et al. *Blood*. 2007;110: Abstract 75. 4. Waage A, et al. *Blood*. 2007;110: Abstract 78. 5. Wijermans P, et al. *Haematologica*. 2008;93: Abstract 0440.

MP-Thal: 35% Reduced Risk of Progression (14% to 50%)
ASCT: 25% Reduced Risk of Progression (4% to 41%)

MP vs MP-Thal

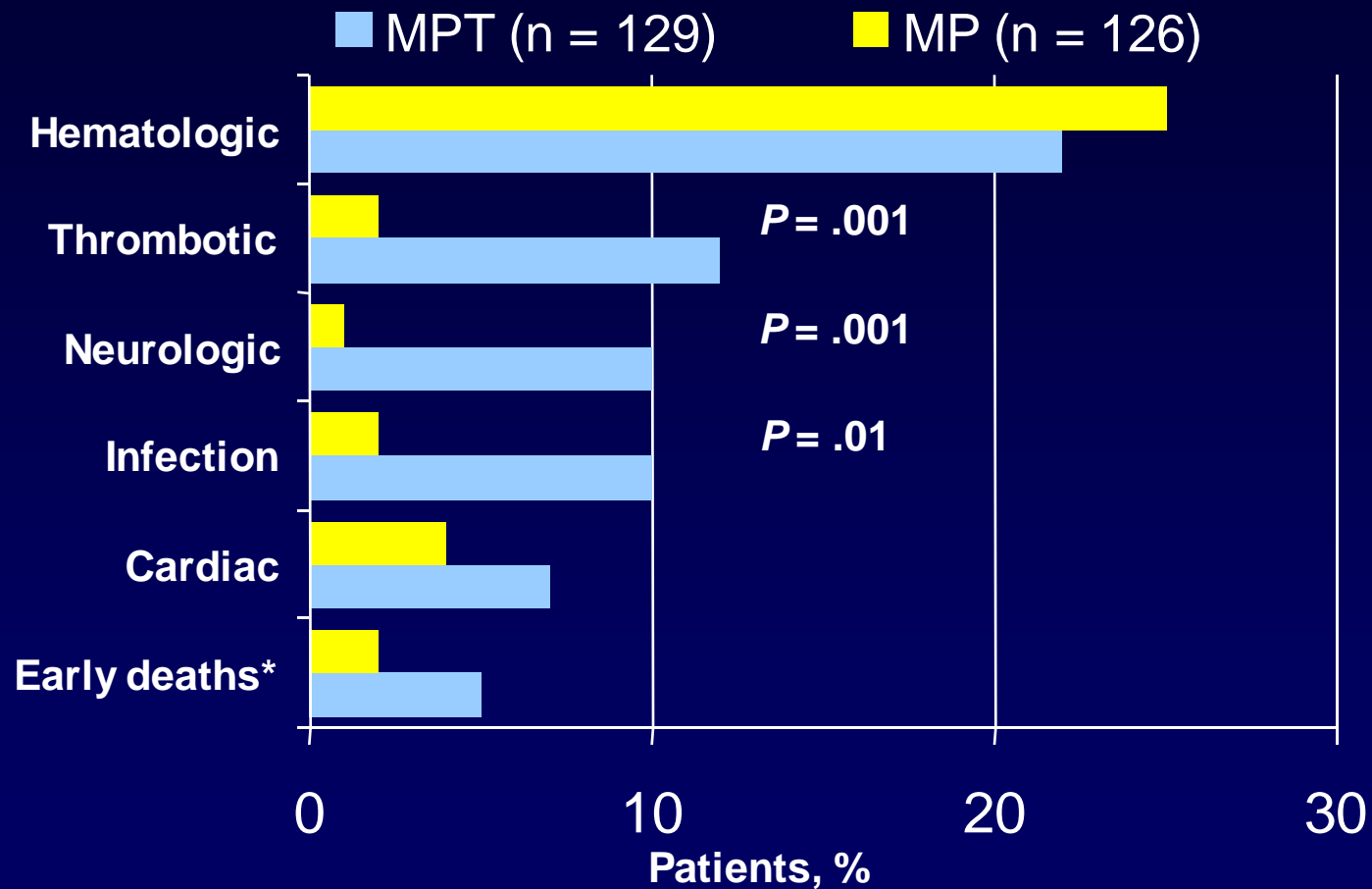


MP-Thal vs ASCT



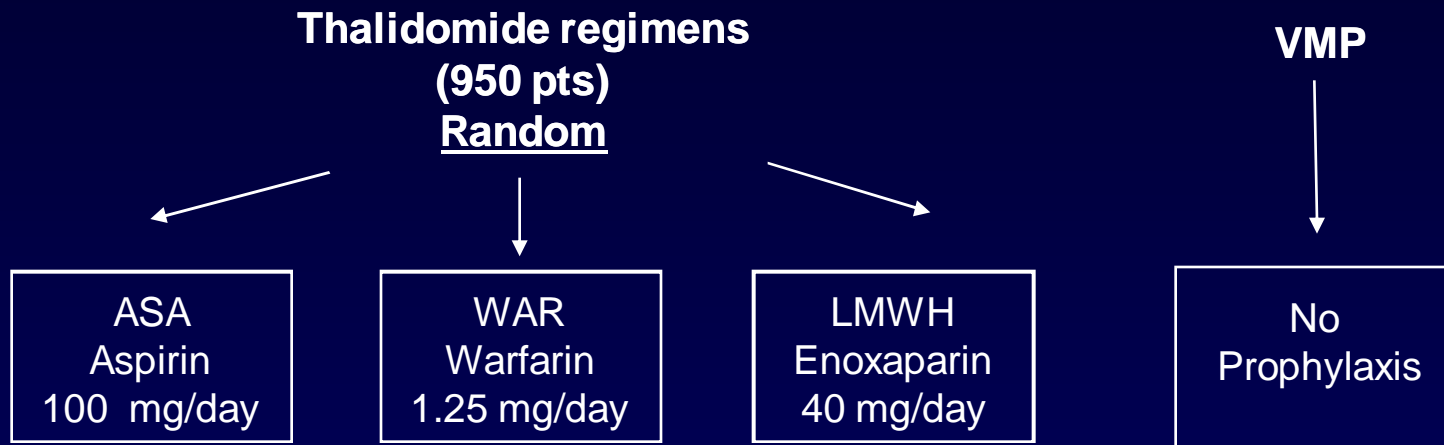
1. Facon T, et al. *Lancet*. 2007;370(9594):1209-1218. 2. Palumbo A, et al. *Lancet*. 2006;367(9513):825-831. 3. Hulin C, et al. *J Clin Oncol*. 2007;25(18S): Abstract 8001. 4. Gulbrandsen N, et al. *Haematologica* 2008;93: Abstract 0209. 5. Koreth J, et al. *Biol Blood Marrow Transplant*. 2007;13(2):183-196.

MPT in Elderly Patients: Grade 3/4 AEs

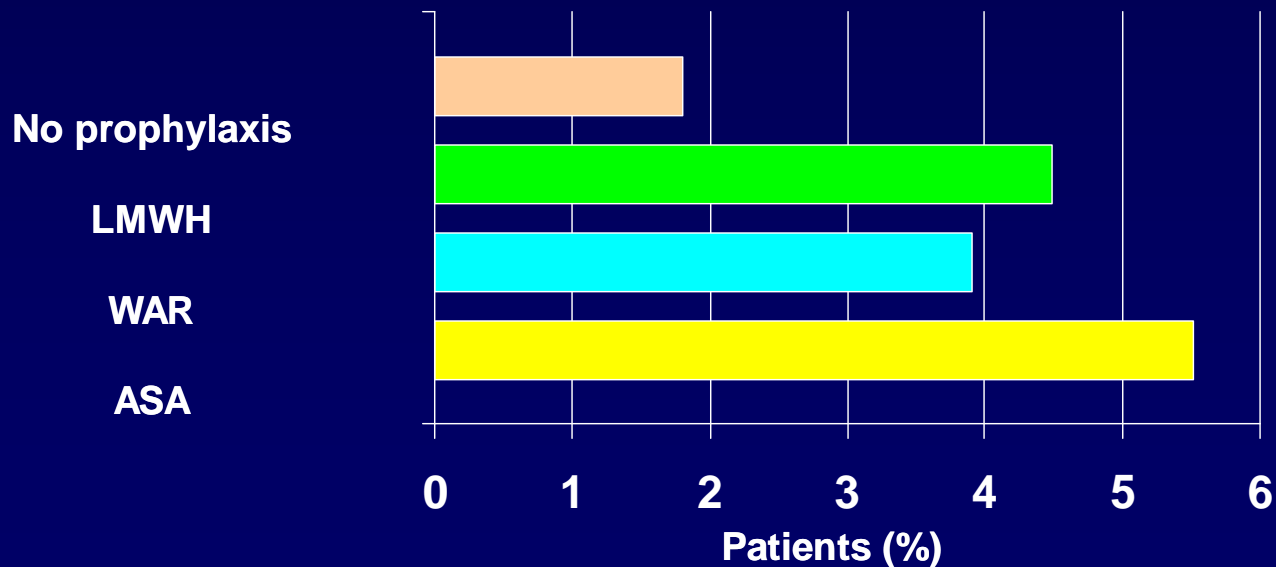


LMWH vs Warfarin vs ASA Prophylaxis for Thalidomide Regimens:

Study Design

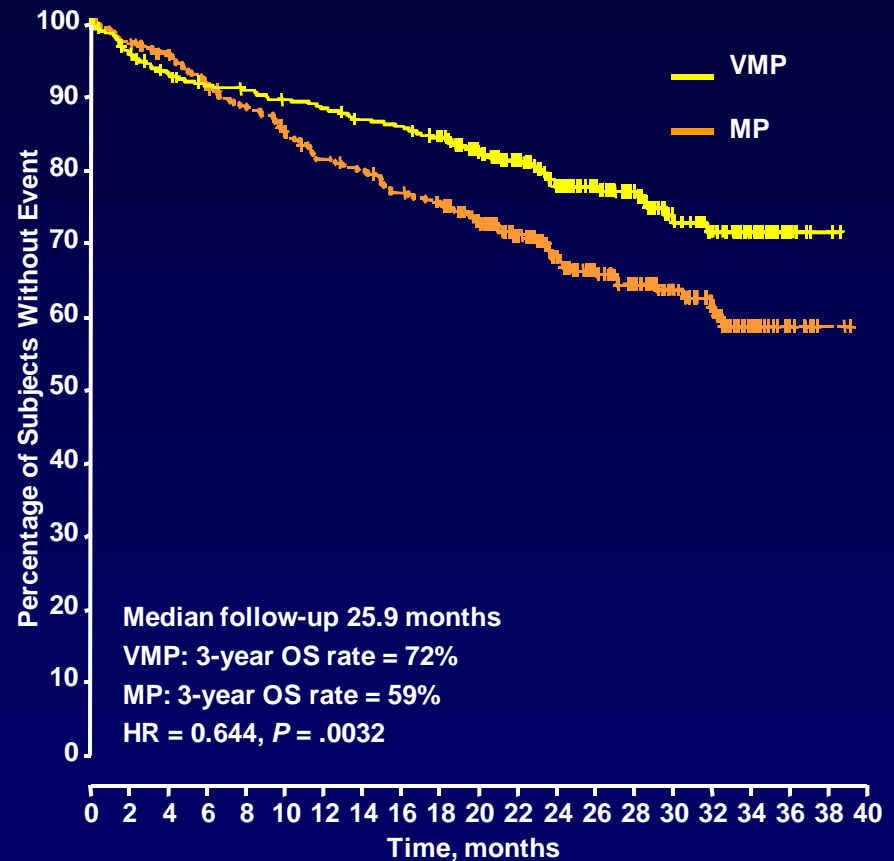
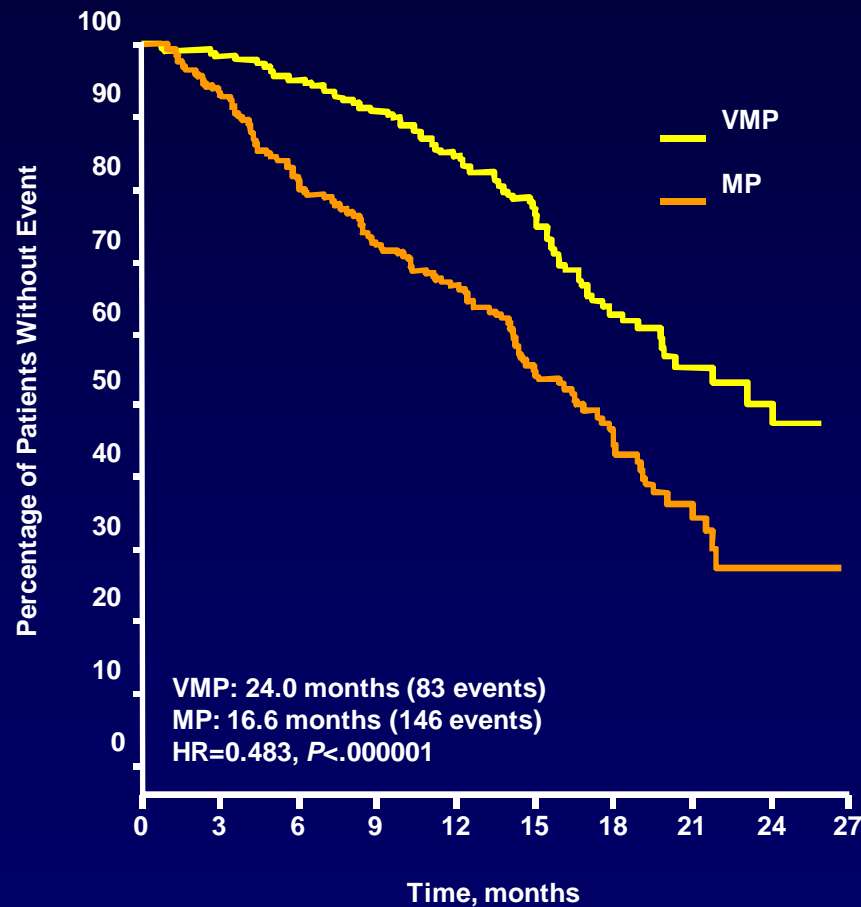


Rates of VTE

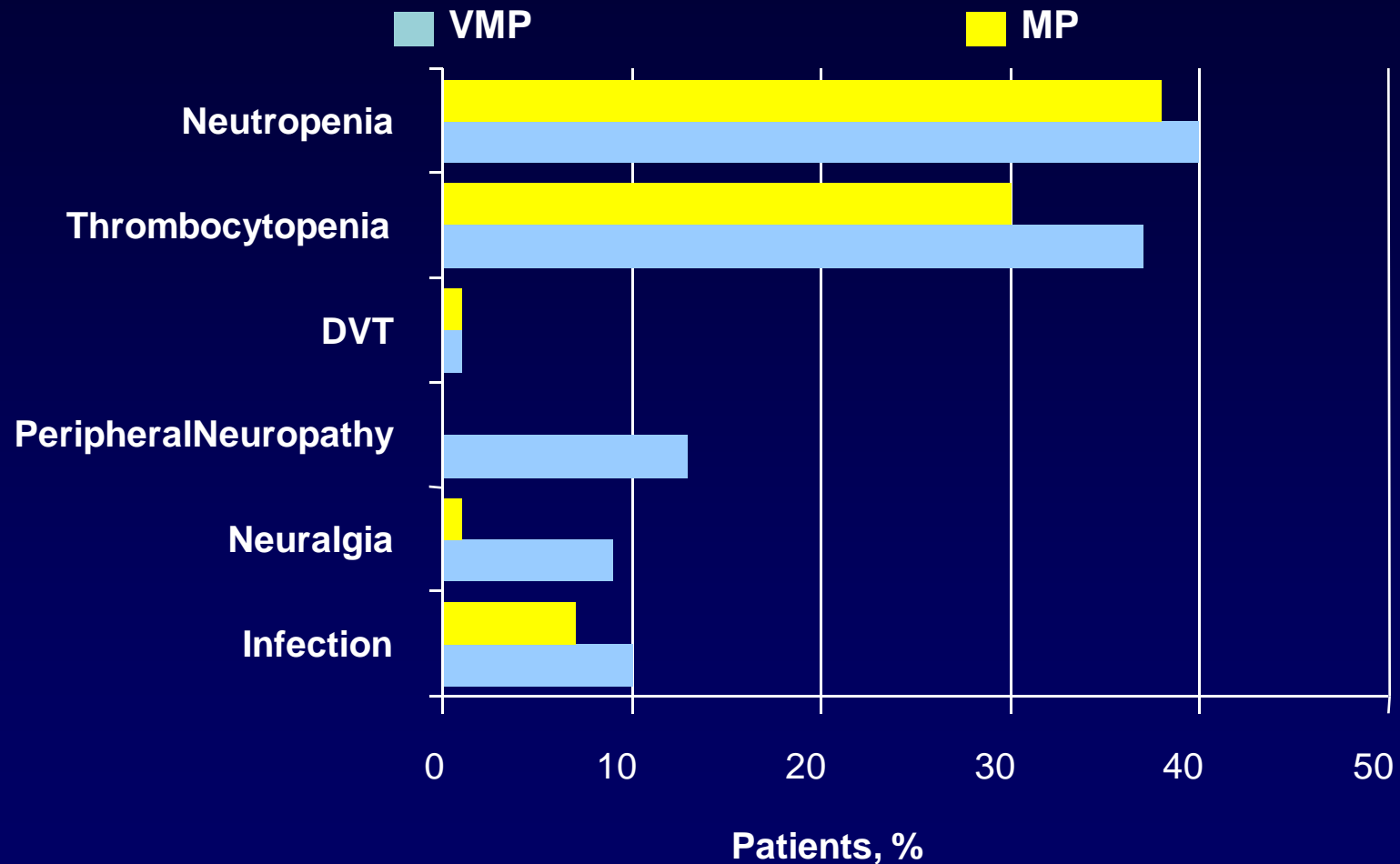


MPV: The Current Standard of Care in Transplant Ineligible Patients

52% reduced risk of progression
~36% reduced risk of death



VMP in Elderly Patients: Grade 3/4 AEs

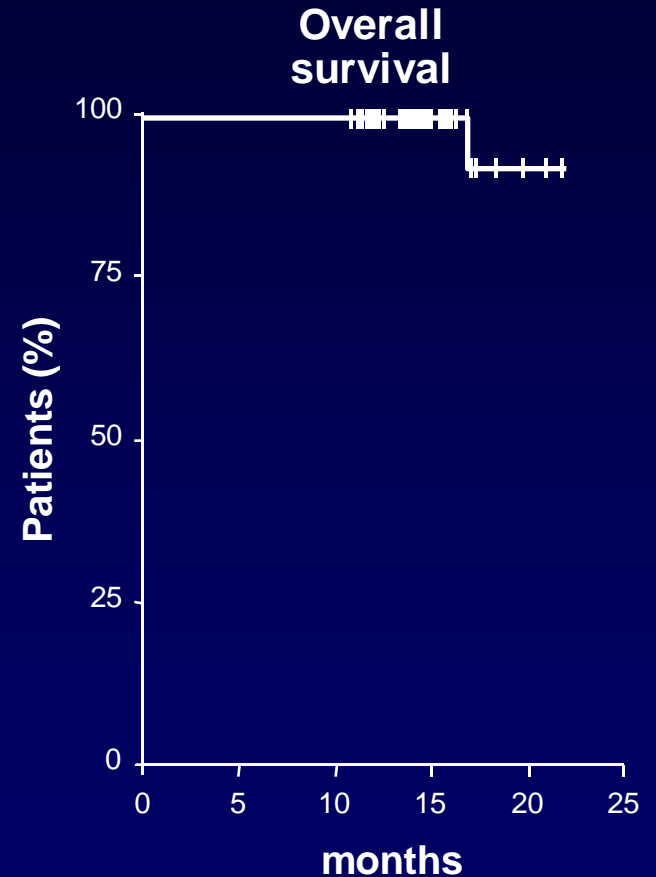
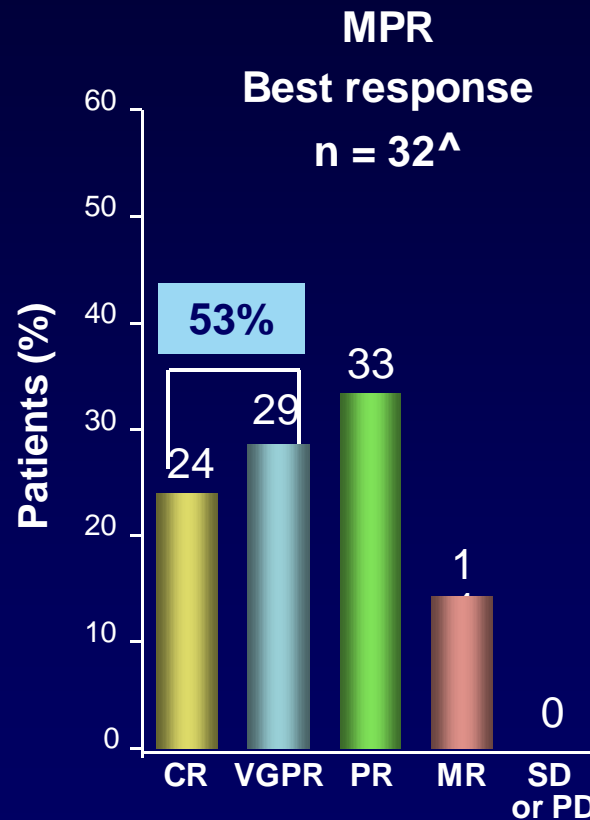
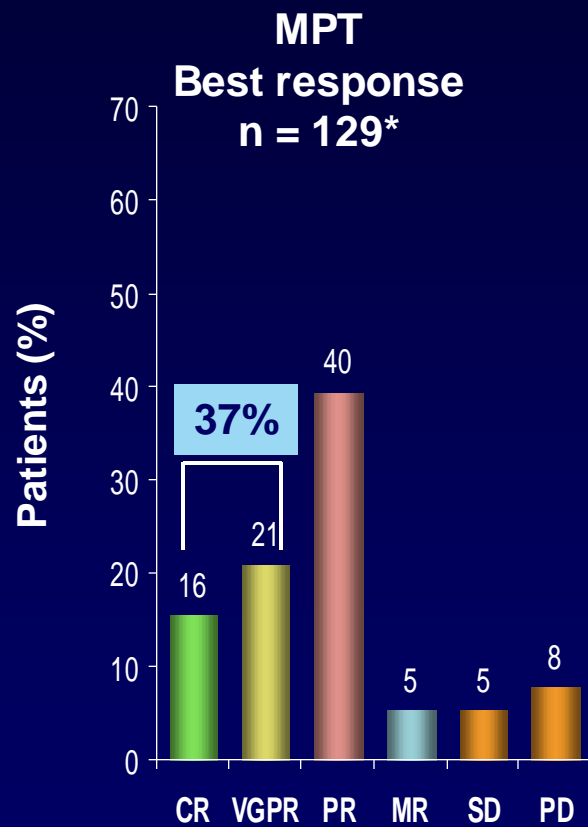


San Miguel JF, et al. *N Engl J Med.* 2008;359(9):906-917.

VMP: Biweekly or Weekly Infusion?

	VMP Biweekly (N = 42)	VMP Mix (N = 19)	VMP Weekly (N = 116)
CR	27%	23%	20%
Peripheral sensory neuropathy	14%	16%	2%
Neuralgia	12%	10%	3%
Discontinuation	24%	22%	10%

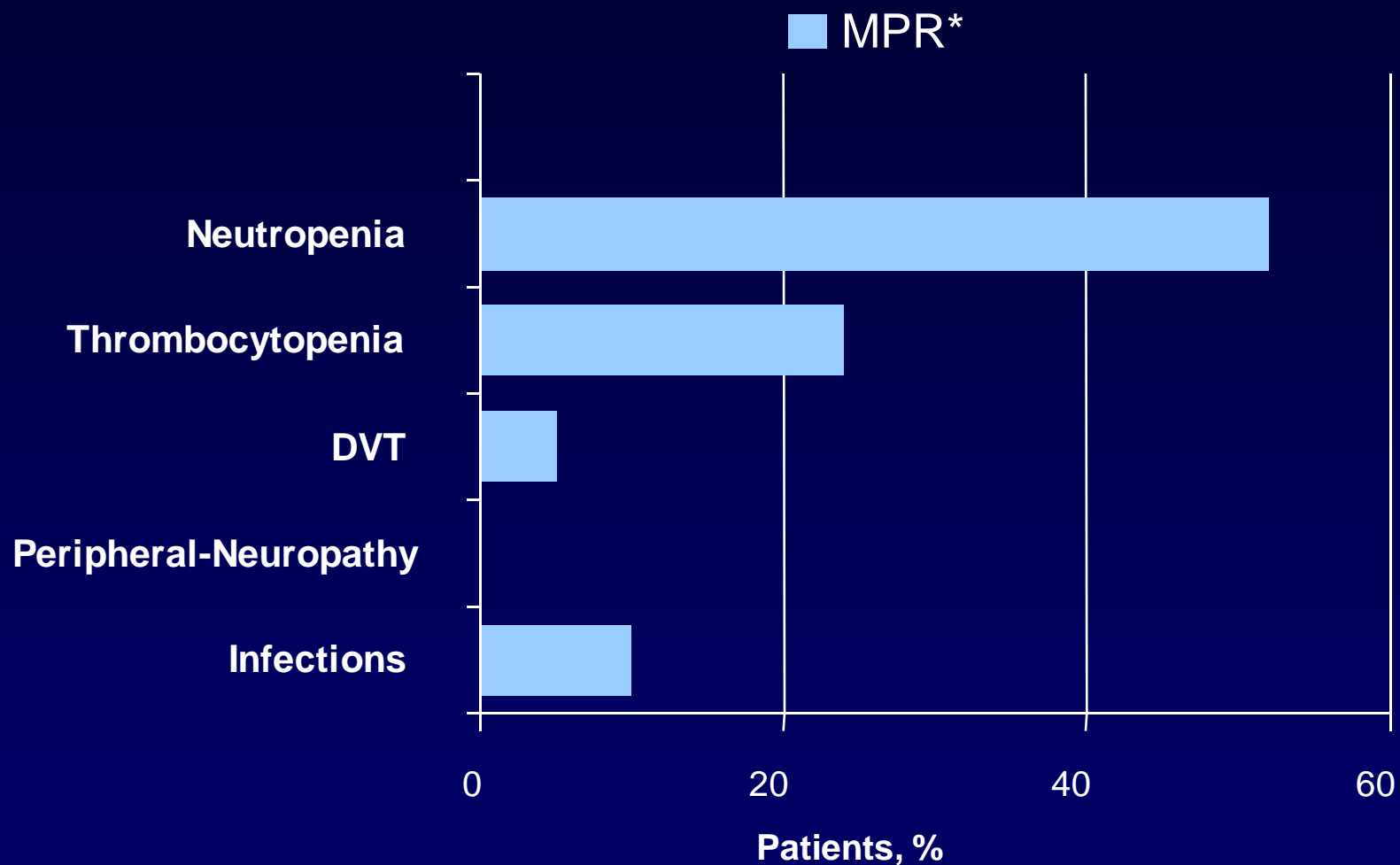
Response: MPT versus MPR



*Palumbo A, et al. *Lancet*. 2006;367(9512):825-831.

^Palumbo A, et al. *J Clin Oncol*. 2007;25(28):4459-6445.

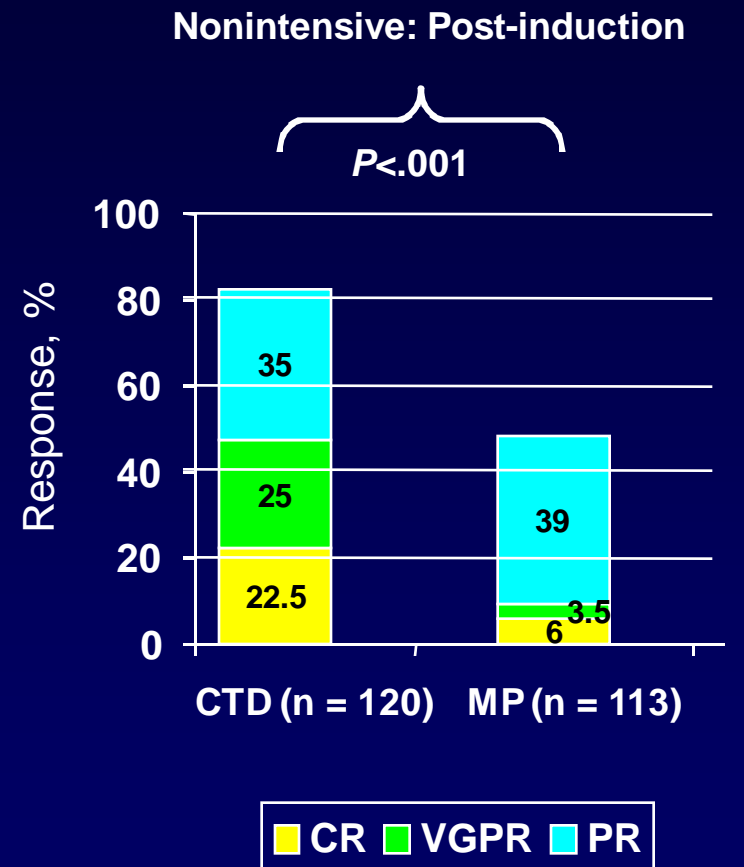
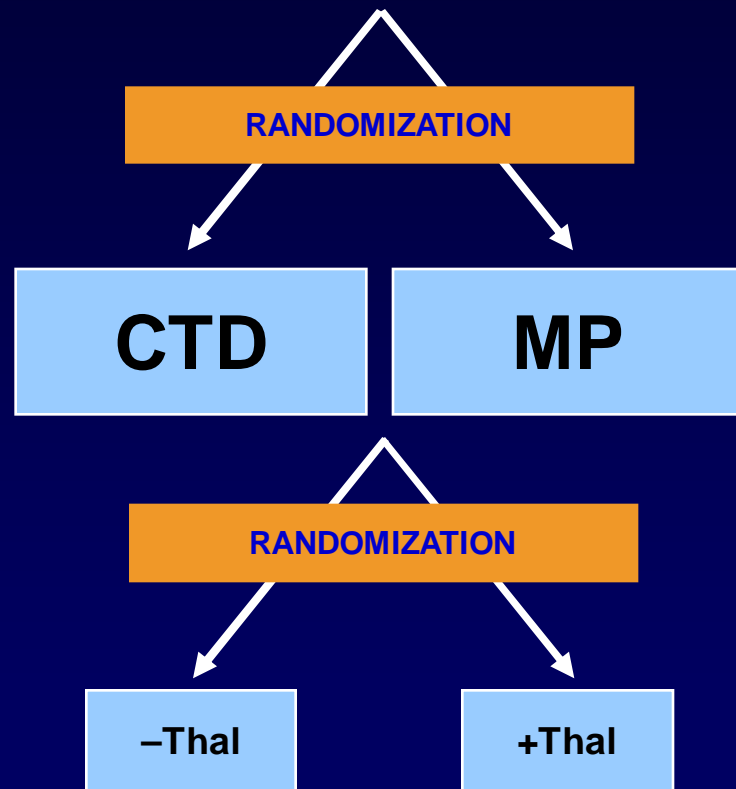
MPR: Grade 3/4 AEs



*Melphalan 0.18 mg/kg, days 1–4; Prednisone 2 mg/kg, days 1–4; Lenalidomide 10 mg/day, days 1–21

Palumbo A. et al. *J Clin Oncol.* 2007;25(28):4459-4465.

CTD vs MP in Newly Diagnosed MM: MRC Myeloma IX Study



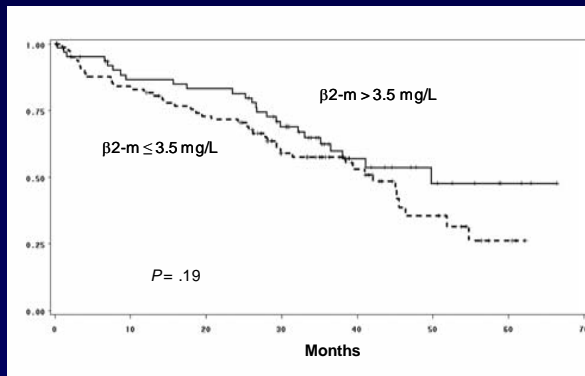
CTD, cyclophosphamide, 500 mg po days 1, 8 and 15; thalidomide 50–200 mg/day; dexamethasone 20 mg/day po days 1–4, 15–18 q 4 wk

Morgan GJ, et al. *Blood*. 2007;110: Abstract 3593.

Prognostic Factors

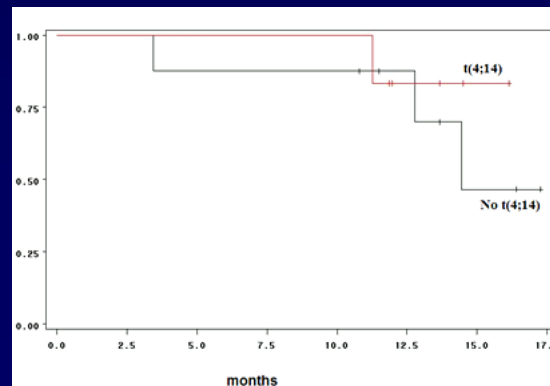
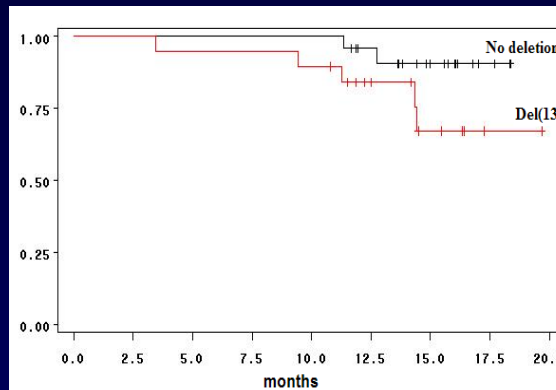
MPT

$\beta 2$ -microglobulin > 3.5 mg/dL



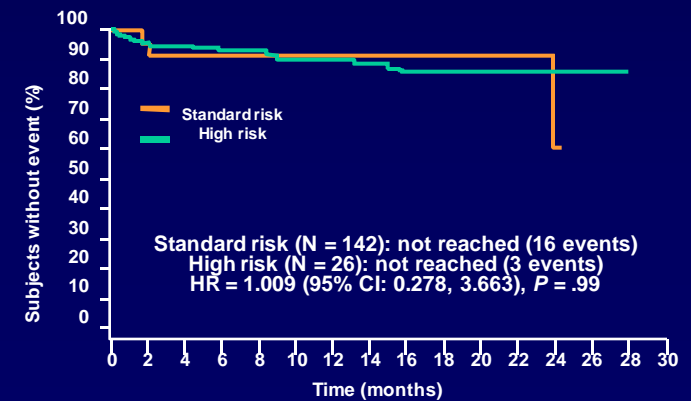
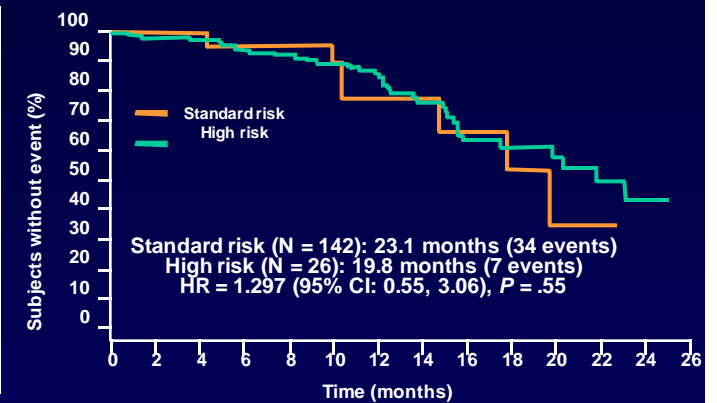
MPR

Del 13; t(4;14)



MPV

t(4;14), t(14;16), del 17p



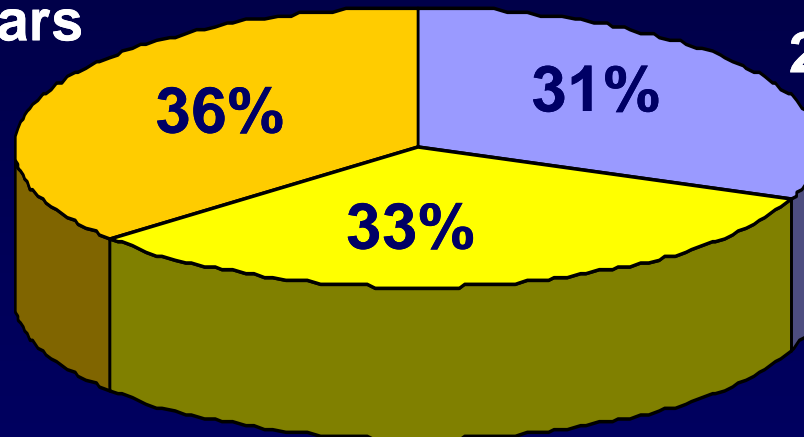
Age-Adjusted Therapy

Full dose
chemotherapy

Autologous
transplant

65-75 years

25-64 years



75-101 years

Reduced-dose
chemotherapy

Early Discontinuation

	ITT Doses	Starting Dose	Early Discontinuation, %
MPT¹ Thalidomide	400 mg/d	200 mg/d in 52% pts	45%
MPT² Thalidomide	100 mg/d	100 mg/d	41%
VISTA³ Bortezomib	1.3mg/m ² d1,4,8,11	1.3mg/m ² d1,4,8,11	34%

1. Facon T, et al. *Lancet* .2007; 370(9594):1209-1218. 2. Palumbo A, et al. *Lancet*. 2006;367(9512):825-831. 3. San Miguel J, et al. *N Engl J Med*. 2008;359(9):906-917.

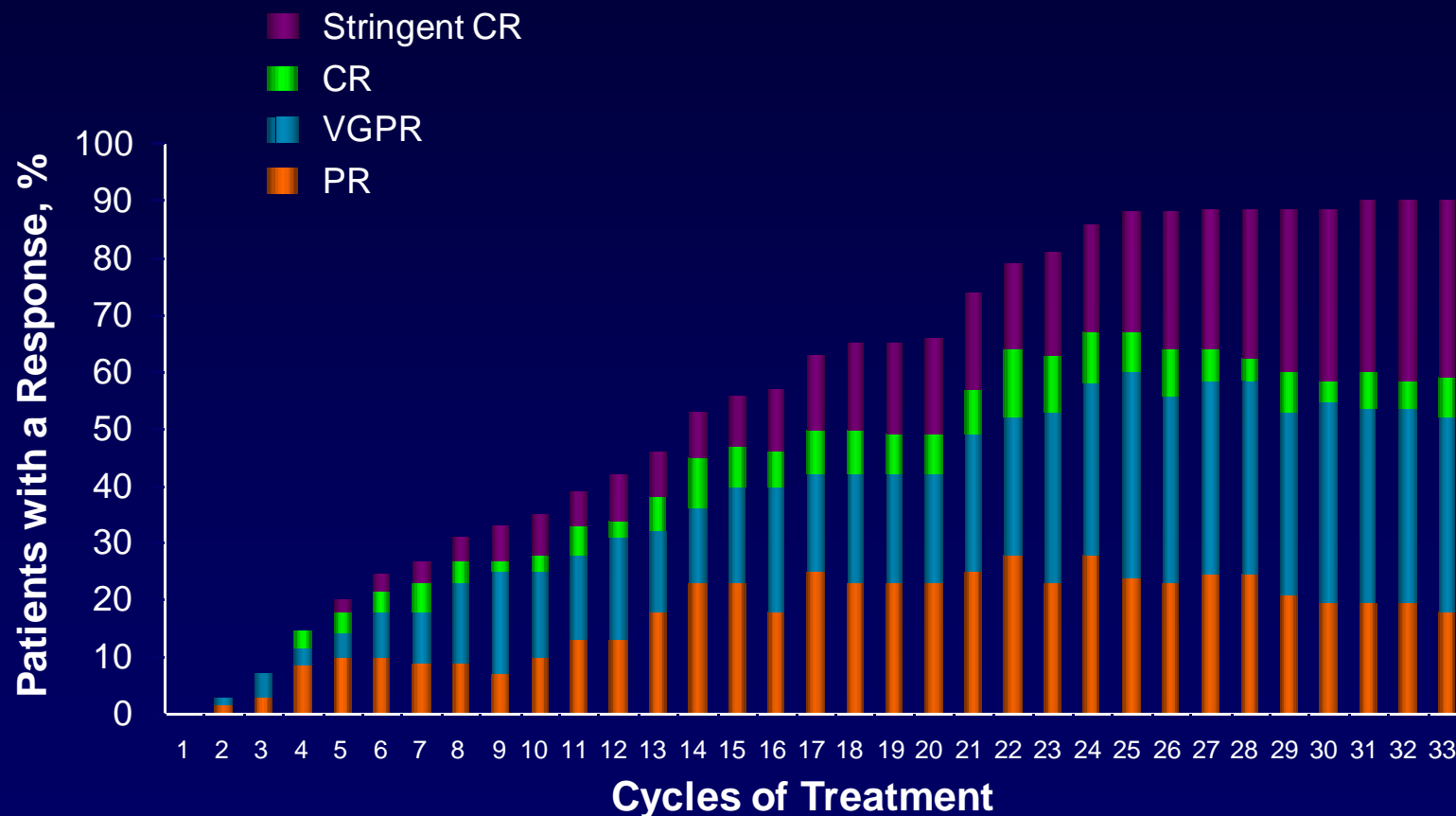
Age-Adjusted Doses

	65-75 Years	>75 Years	Further Dose Redcution
Dexamethasone weekly	40 mg	20 mg	10 mg
Melphalan days 1-4	0.25 mg/kg	0.18 mg/kg	0.13 mg/kg
Thalidomide per day	200 mg	100 mg	50 mg
Lenalidomide* days 1-21	25 mg	15 mg	10 mg
Bortezomib	1.3 mg/m ² biweekly	1.3 mg/m ² weekly	1.0 mg/m ² weekly

If a grade 3-4 AE occurs: 1. discontinue therapy; 2. wait for grade 1 AE; 3. restart at a lower dose

*Lenalidomide plus melphalan starting dose 10 mg/d

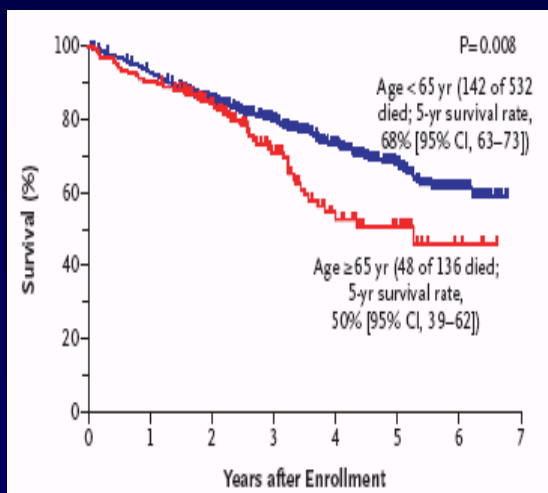
BiRD: Continued Therapy Increases the Quality of the Response



Niesvizky R, et al. *Blood*. 2008;111:1101-1109.

Autologous Stem Cell Transplant in Elderly Patients

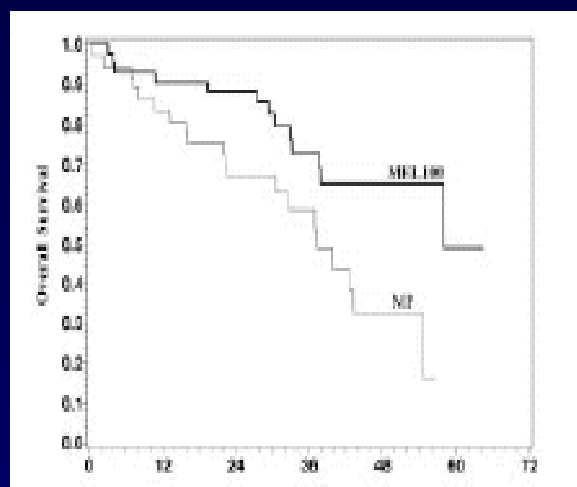
Survival Advantage
Age <65 years



Tandem MEL200

Barlogie B, et al. *N Engl J Med.* 2006;354(10):1021-1030.

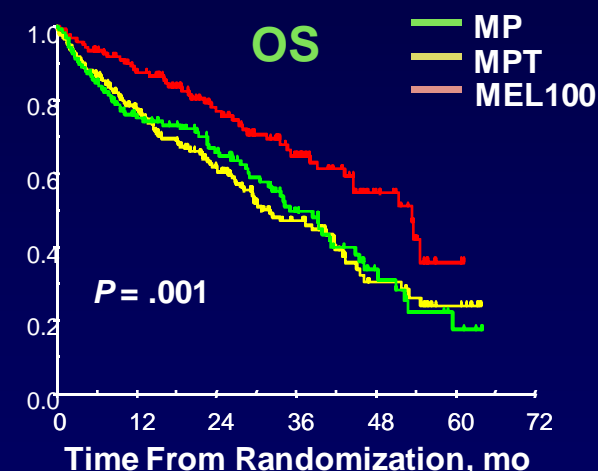
Survival Advantage
Age 65-70 years



Tandem MEL100

Palumbo A, et al. *Blood.* 2004;104:3052-3057.

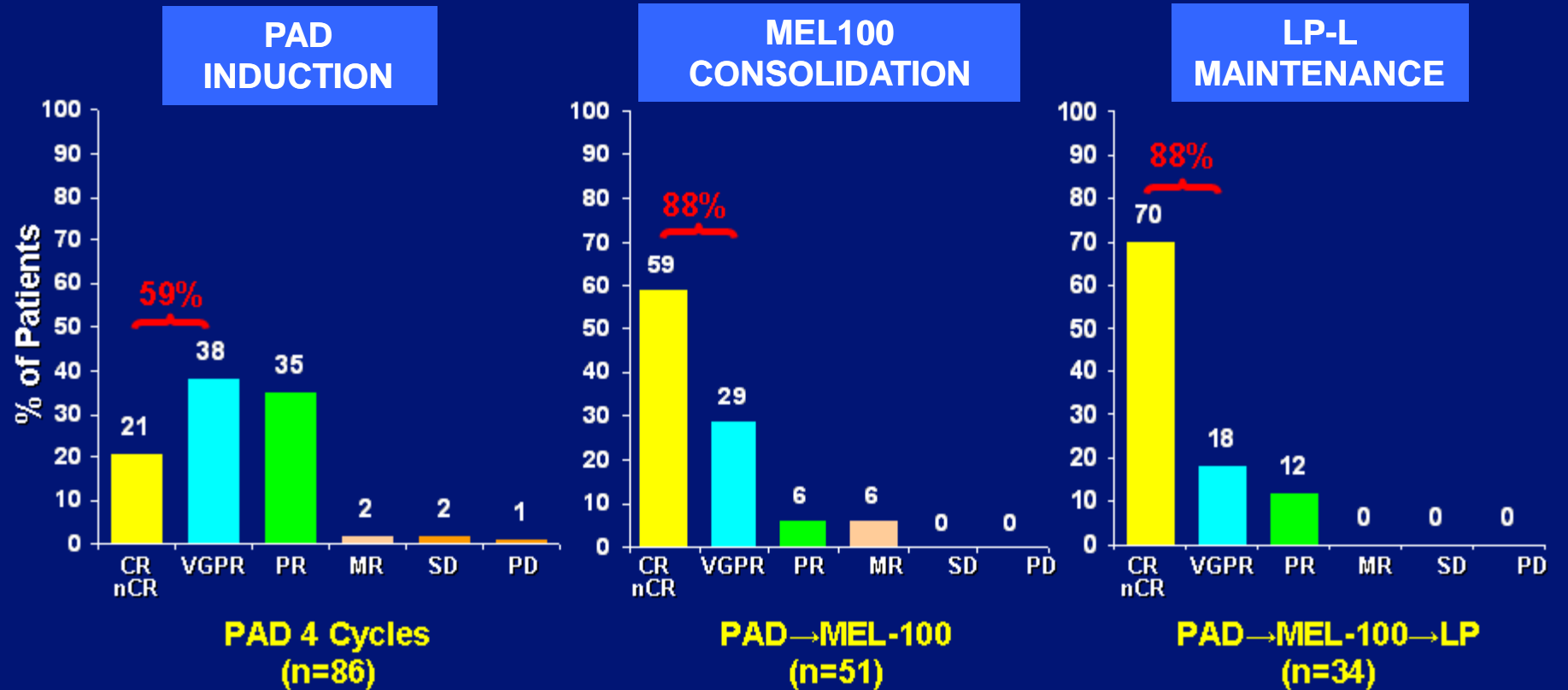
NO Survival Advantage
Age 65-75 years



Tandem MEL100

Facon T, et al. *Lancet.* 2007;370(9594):1209-1218.

Role of Maintenance After Autologous Transplant



* Per protocol

Palumbo A, et al. *J Clin Oncol*. 2008;26(18S): Abstract 8518; updated results presented at: 44th ASCO Annual Meeting; May 30 – June 3, 2008; Chicago, Illinois.

Therapeutic Algorithm

Level of Evidence 1b (≥ 1 Randomized Trial)

Diagnosis

> 65 years

TD

=

MP

1 randomized trial

MPT

>

MP

5 randomized trials

MPV

>

MP

1 randomized trial

MPR

MP

under evaluation