

GIMEMA: Italian Myeloma Network

A Prospective, Randomized, Phase III Study of Bortezomib, Melphalan, Prednisone and Thalidomide (VMPT)

versus

Bortezomib, Melphalan and Prednisone (VMP) in Elderly Newly Diagnosed Myeloma Patients

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Rationale

	MP¹ (upfront)	MPT² (upfront)	VMP¹ (upfront)	VMPT³ (relapse)
No. patients	331	167	337	30
CR	4%	16%	33%	17%
VGPR	8%	29%	41%	44%
PR	39%	69%	74%	67%

V = Velcade; M= Melphalan; P = Prednisone; T= Thalidomide

¹ San Miguel JF et al. New Eng J Med 2008; 359: 906-17; ² Palumbo et al. Blood 2008;112: 3107-3114

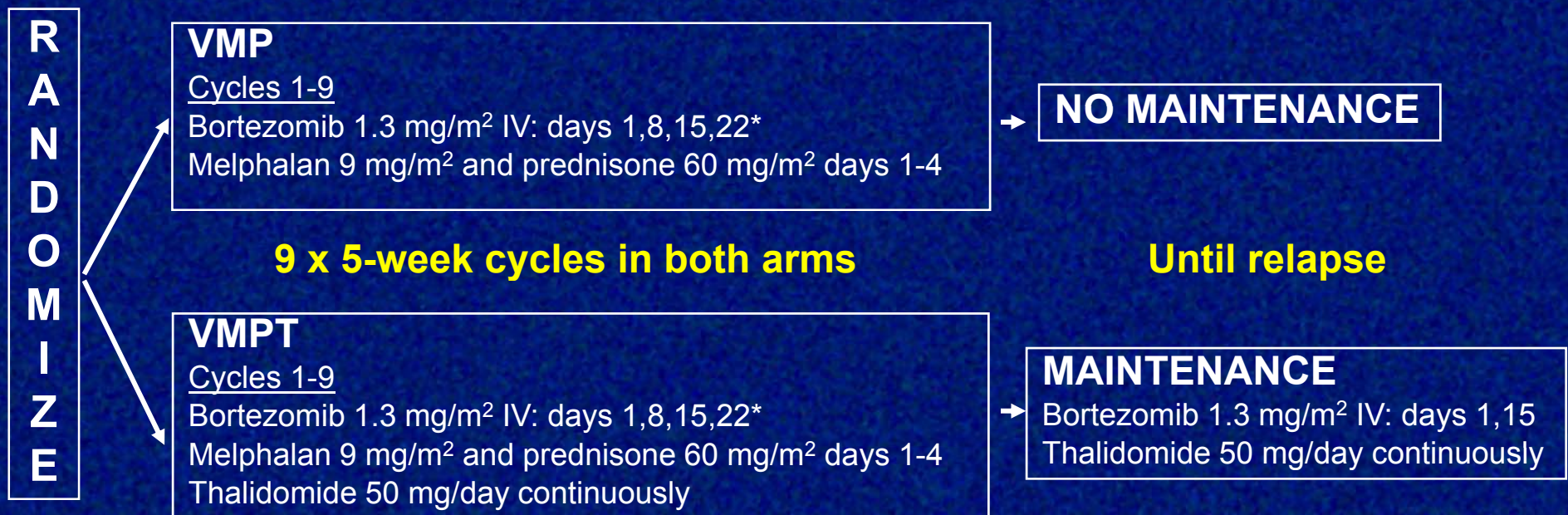
³ Palumbo et al. Blood 2007;109: 2767-2772

Aims

- **VMPT**: superior to VMP?
- **Bortezomib weekly infusion**: safety improvement?

Treatment schedule

- 393 patients (older than 65 years) randomized from 58 Italian centers
- Patients: Symptomatic multiple myeloma/end organ damage with measurable disease
 - ≥ 65 yrs or < 65 yrs and not transplant-eligible; creatinine ≤ 2.5 mg/dL



* 61 VMP patients and 70 VMPT patients were treated with biweekly infusions of Bortezomib

Patient Characteristics

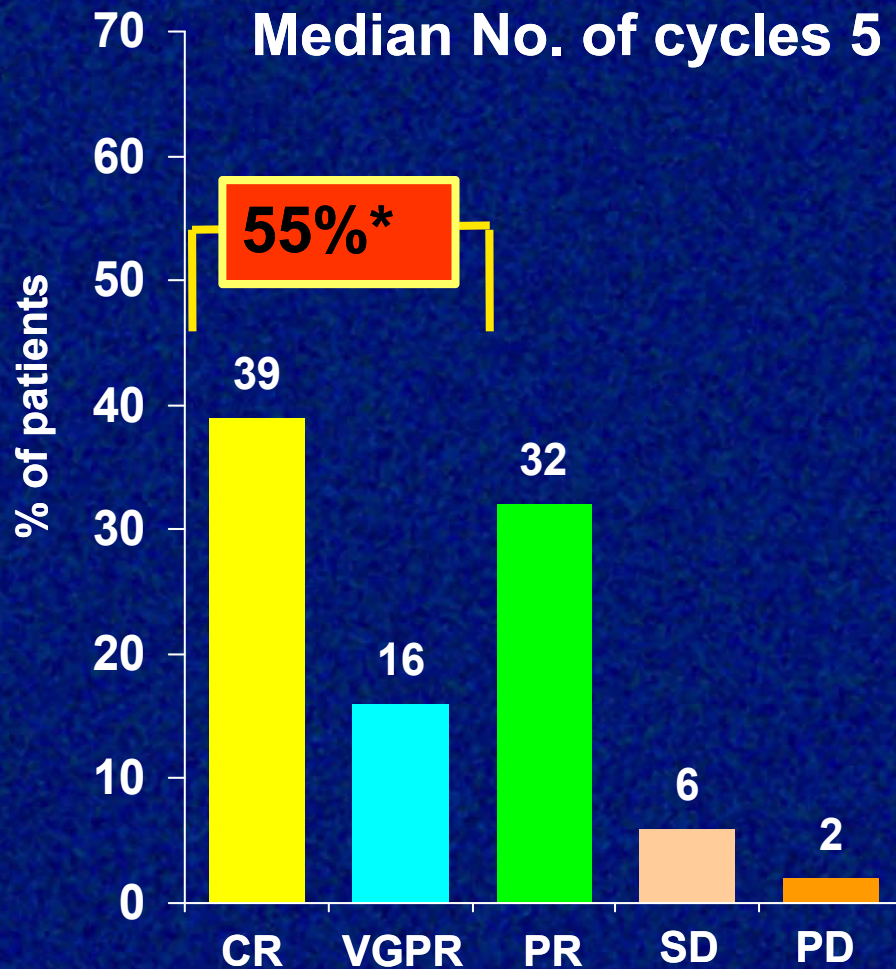
	VMPT (n=177)	VMP (n=177)
Age (median)	71	72
≤70 years	49%	42%
71–75 years	31%	34%
>75 years	20%	25%
β2-microglobulin-mg/L (median)	3.7	4.0
Hemoglobin-g/dL (median)	10.9	10.6
Creatinine-mg/dL (median)	1.0	1.1
Calcemia-mmol/L (median)	2.32	2.32

Best Response

VMPT

N=177

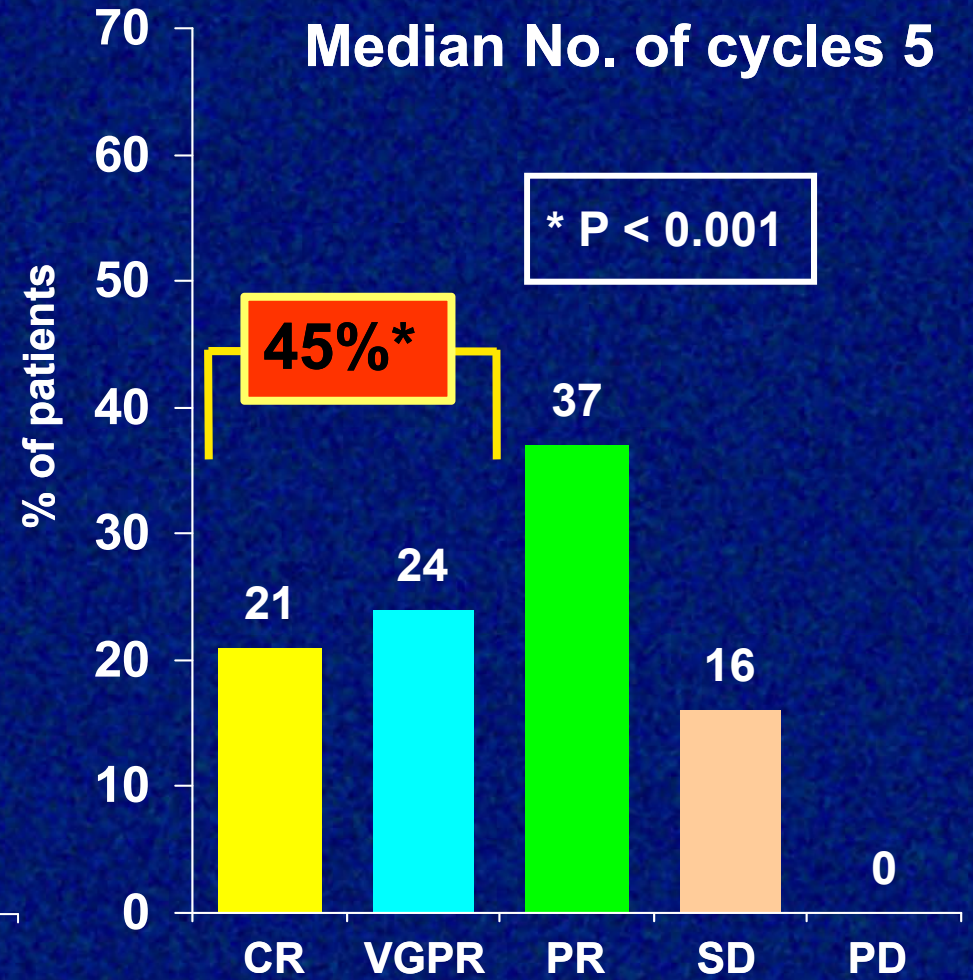
Median No. of cycles 5



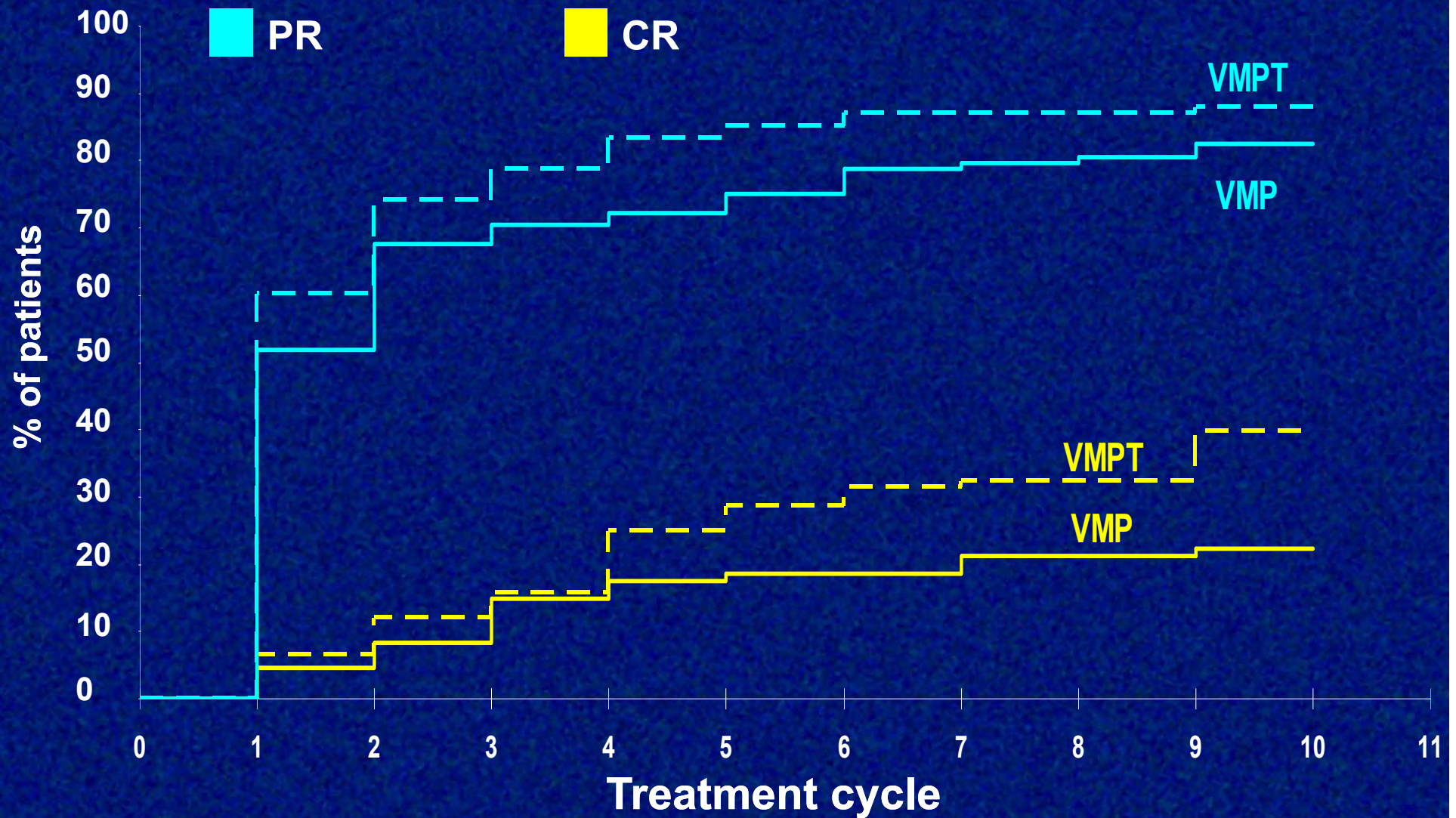
VMP

N=177

Median No. of cycles 5



Time to response

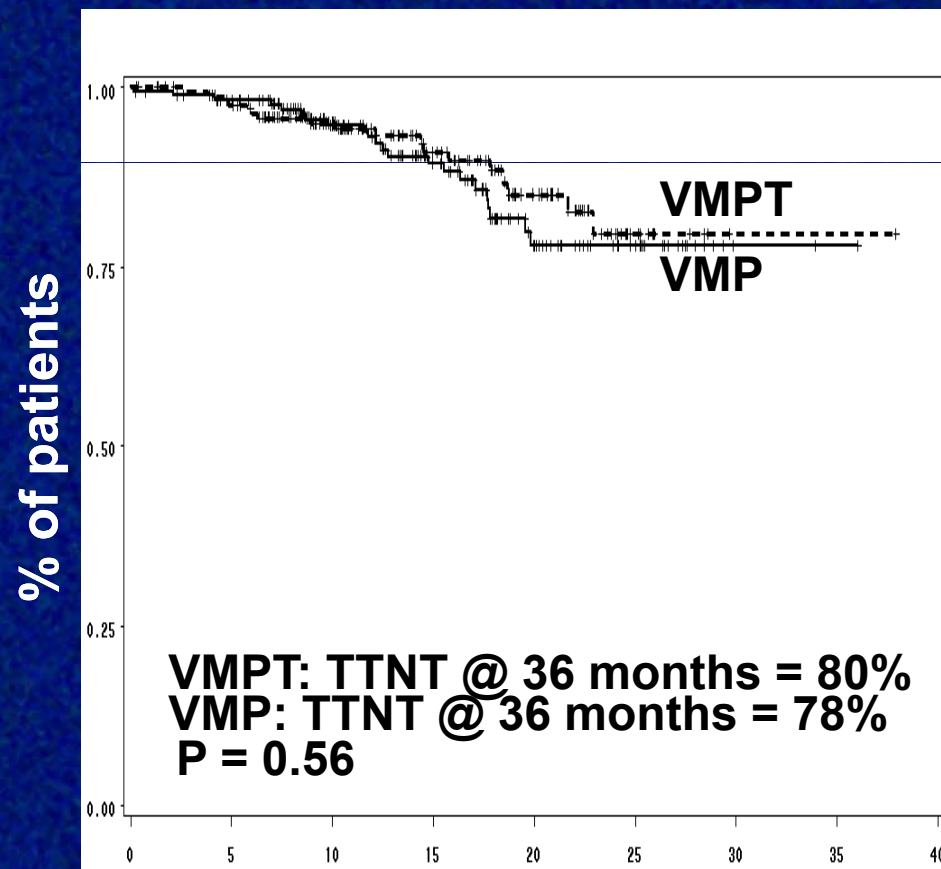


Time to next therapy Progression free survival

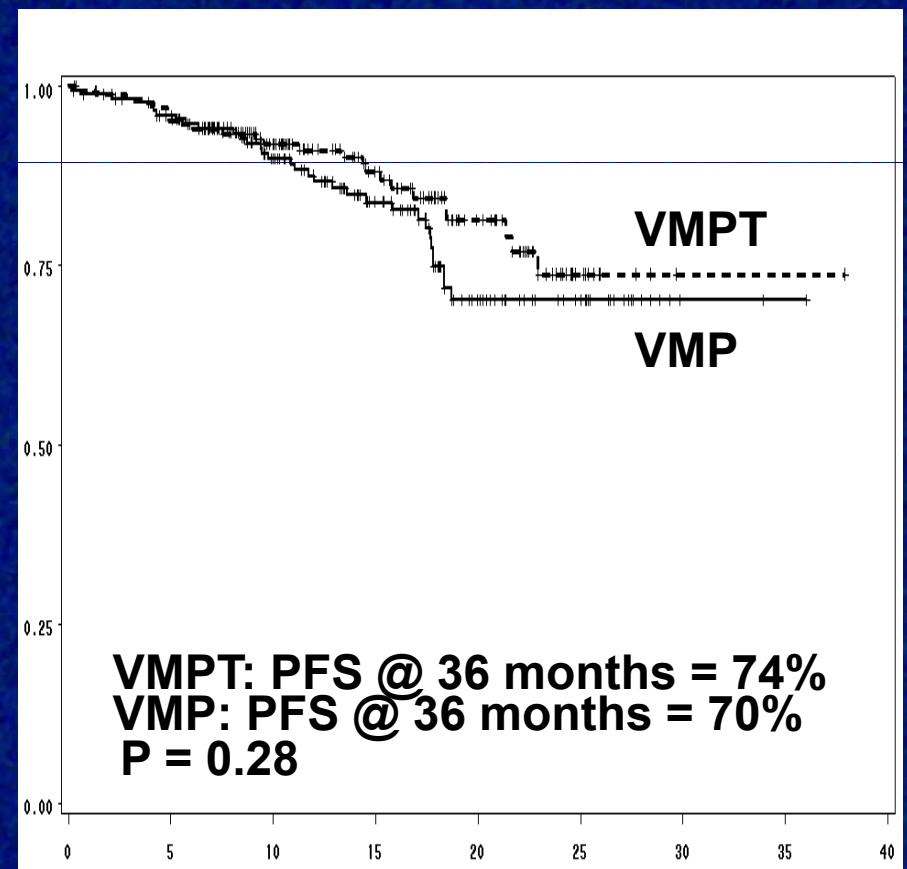
Median follow-up 14.5 months

Time to next therapy

Progression free survival



Months

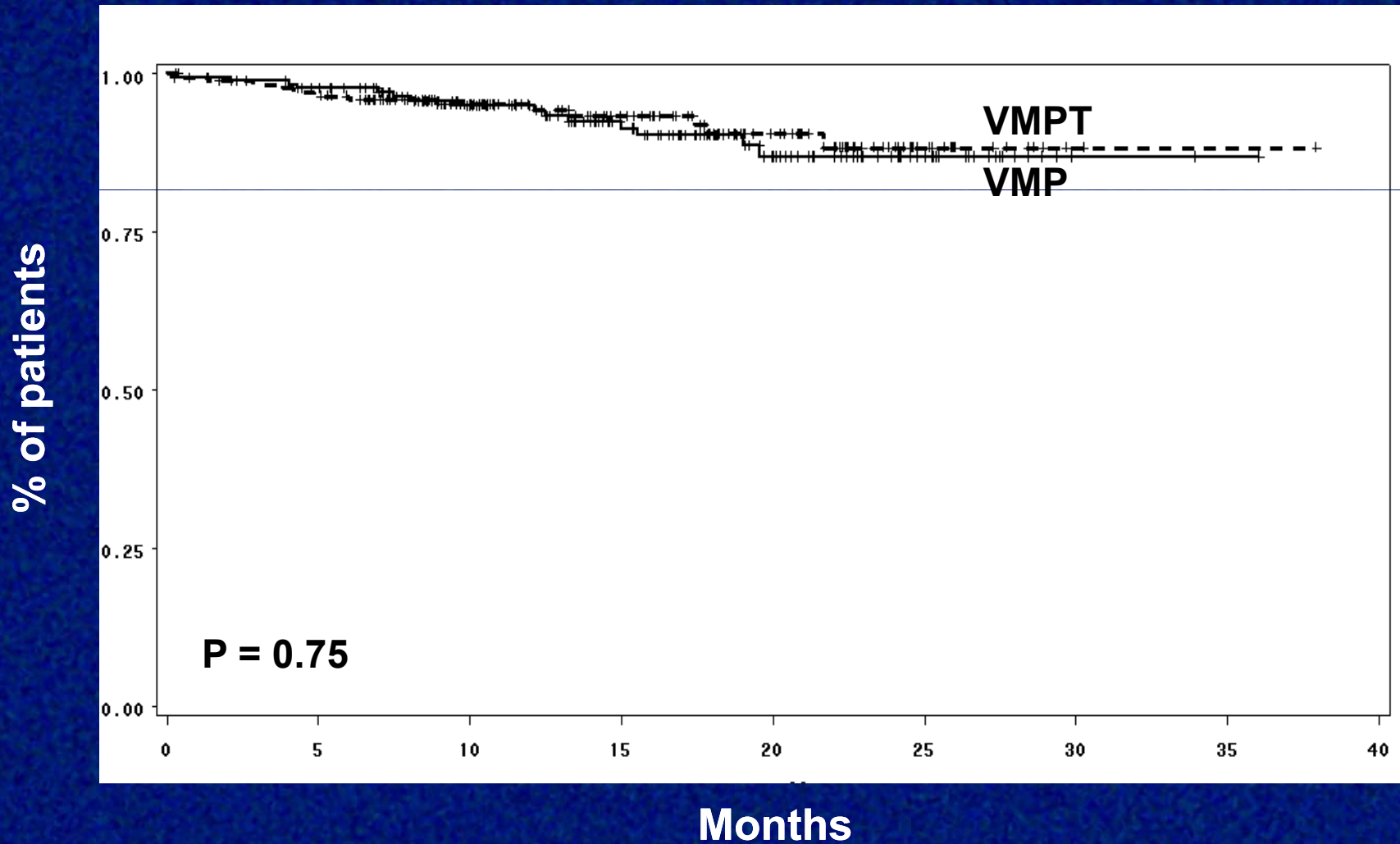


Months

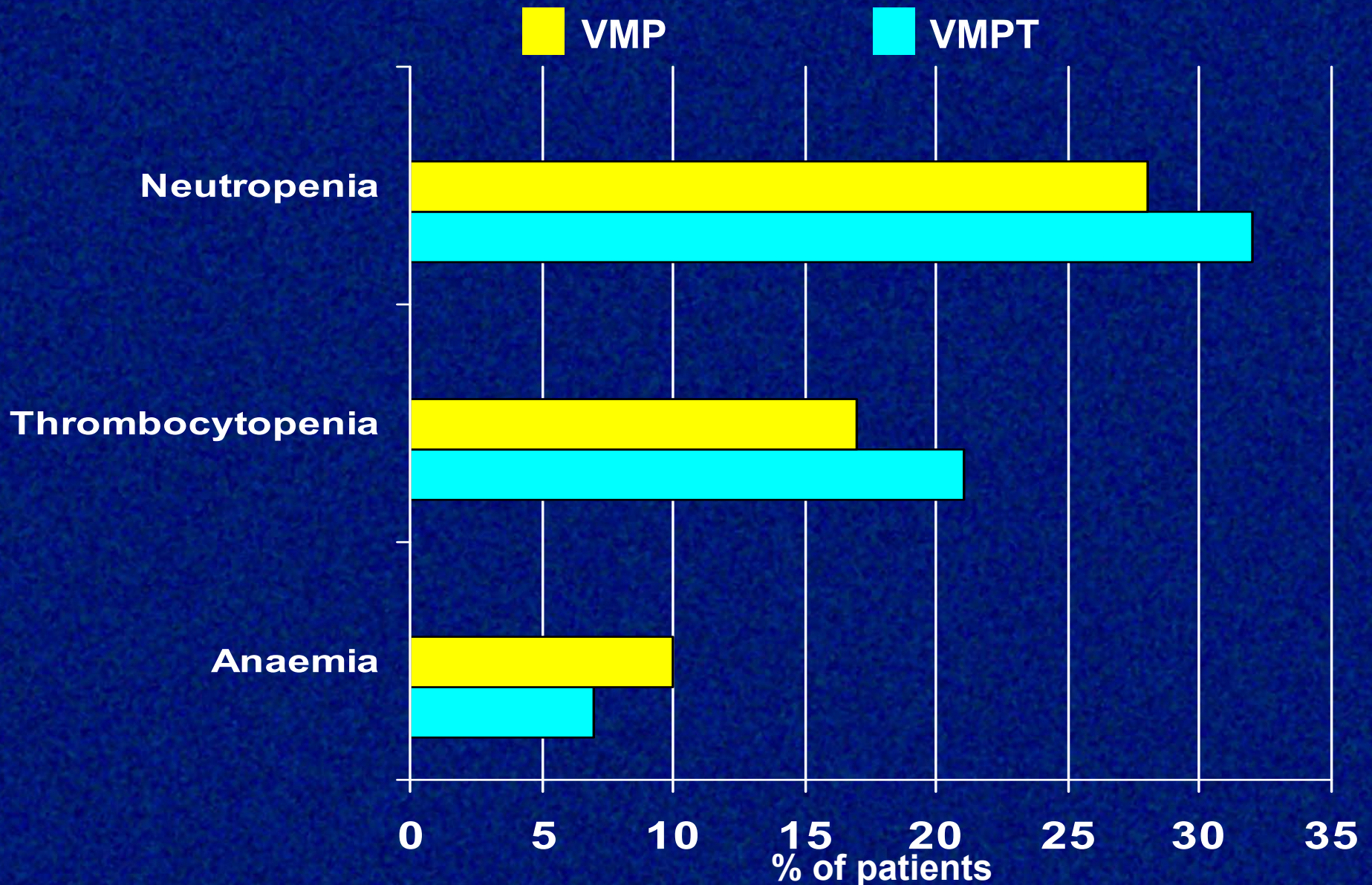
Overall survival

VMPT: OS @ 36 months = 88%

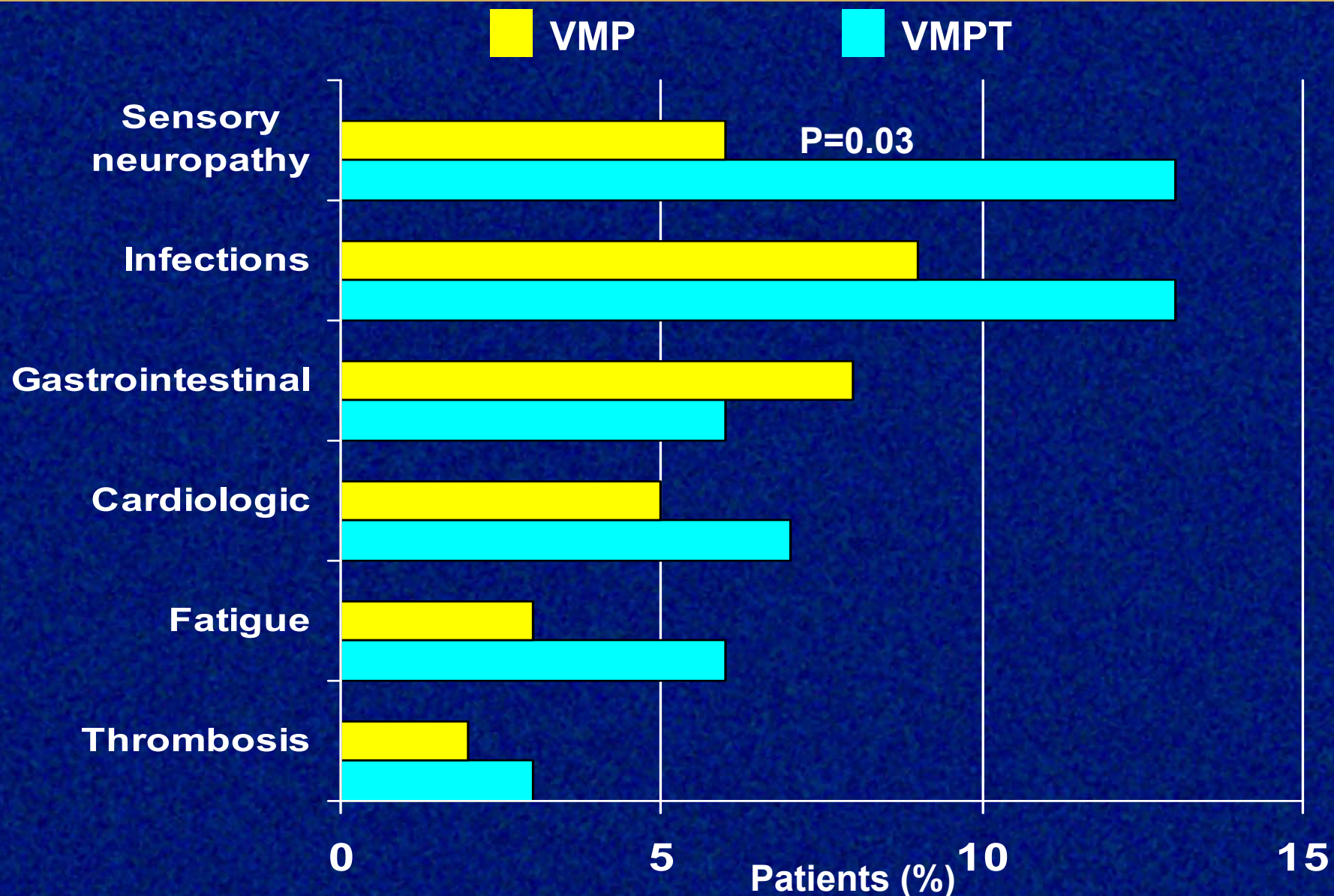
VMP: OS @ 36 months = 87%



Grade 3-4 Hematologic Adverse Events



Grade 3-4 Non-hematologic Adverse Events



Efficacy and Toxicity biweekly – weekly*

	VMPT biweekly (N=45)	VMPT weekly (N=107)	VMP biweekly (N=42)	VMP weekly (N=116)
CR	36%	39%	27%	20%
Peripheral sensory neuropathy	24%	6%	14%	2%
Neuralgia	4%	3%	12%	3%
Discontinuation	22%	10%	24%	10%

*25 VMPT and 19 VMP patients received both biweekly and weekly infusions

Conclusions

	VMPT (N=177)	VMP (N=177)	P value
CR	39%	21%	< 0.001
≥ VGPR	55%	45%	< 0.001
TTNT @ 3 years	80%	78%	0.56
PFS @ 3 years	74%	70%	0.28
OS @ 3 years	88%	87%	0.75

Conclusions 2

- VMPT improves response rates of VMP
- Weekly infusion of bortezomib decreases peripheral neuropathy
- Longer follow-up is needed to assess PFS and OS

We Are Grateful to All Patients, Nurses and Physicians of the Participating Centers

1. ALESSANDRIA	Levis, Baraldi	37. FORLI'	Amadori, Gentilini	73. PINEROLO	Griso
2. ANCONA	Leoni, Offidani	38. FROSINONE	Sala	74. PISA	Petrini/Benedetti
3. AOSTA	Di Vito	39. GALLARATE	Ciambelli	75. POTENZA	Ricciuti, Vertone
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27. CIRIE'	Giroto, Freilone	63. NUORO	Gabbas	99. TORINO	Poccardi, Aragno
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29. CREMONA	Morandi	65. PADOVA	Semenzato, Zambello	101. TRIESTE	De Sabbata
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34. FROSINONE	Sala	70. PESARO	Visani, Leopardi	106. VERONA	Pizzolo, Meneghini
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36. GENOVA	Gobbi, Canepa	72. PIACENZA	Cavanna, Lazzaro	108. VITERBO	Montanaro