

# GIMEMA: Italian Multiple Myeloma Network

**Bortezomib, Melphalan, Prednisone and Thalidomide (VMPT)  
followed by maintenance with Bortezomib and Thalidomide  
(VT) for initial treatment of elderly multiple myeloma patients**

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# Disclosures for Palumbo Antonio, MD

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<b>Research Support/P.I.</b>	<b>No relevant conflicts of interest to declare</b>
<b>Employee</b>	<b>No relevant conflicts of interest to declare</b>
<b>Consultant</b>	<b>No relevant conflicts of interest to declare</b>
<b>Major Stockholder</b>	<b>No relevant conflicts of interest to declare</b>
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<b>Scientific Advisory Board</b>	<b>No relevant conflicts of interest to declare</b>

# Aims

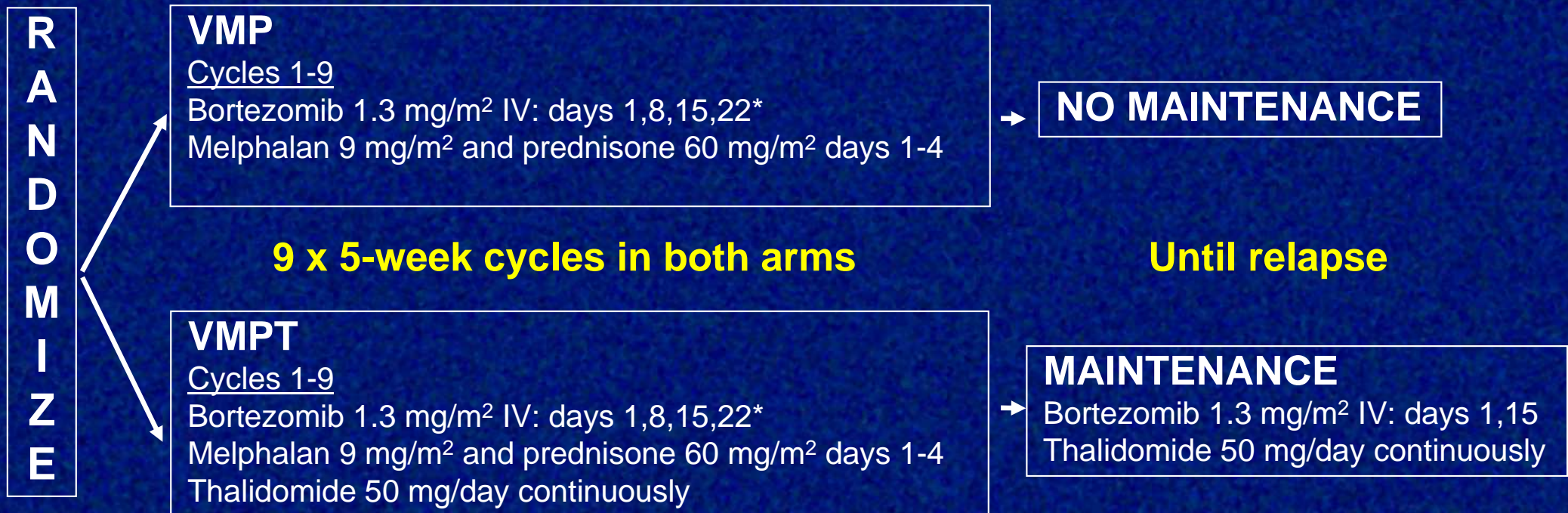
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## Best experimental therapy versus standard of care

- Best experimental therapy:
  - 4 drug combo → VMPT
  - Maintenance → VT
- Best standard of care
  - 3 drug combo → VMP
- Safety and efficacy of weekly infusion of bortezomib

# Treatment schedule

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



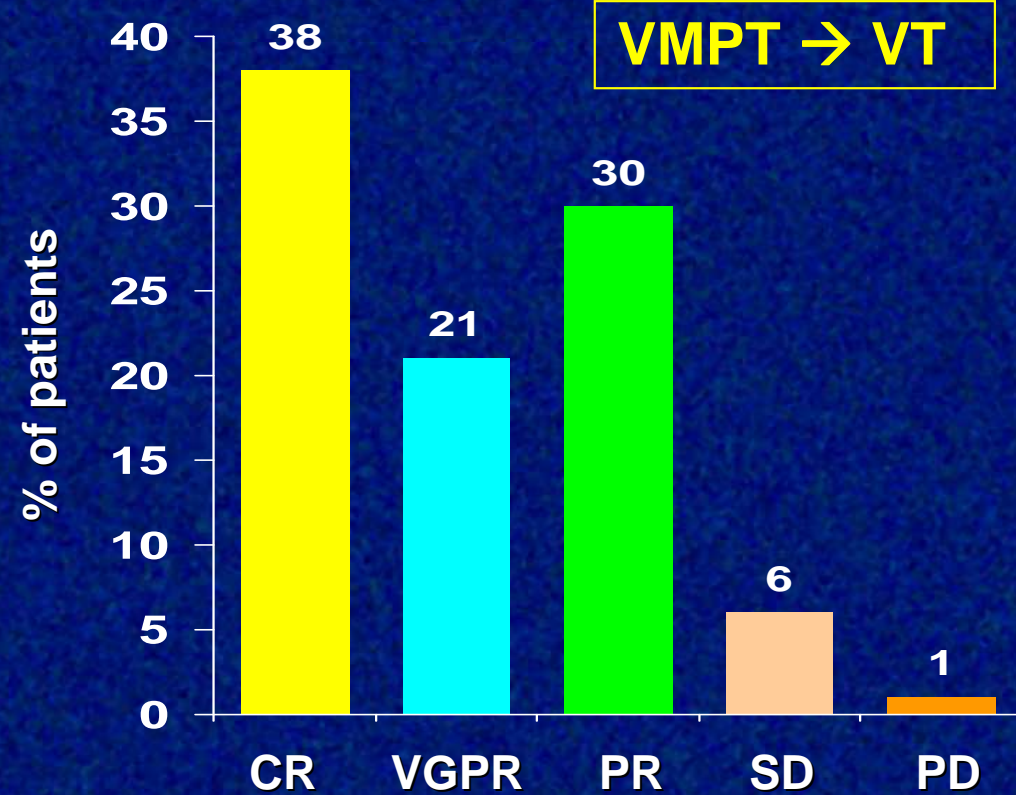
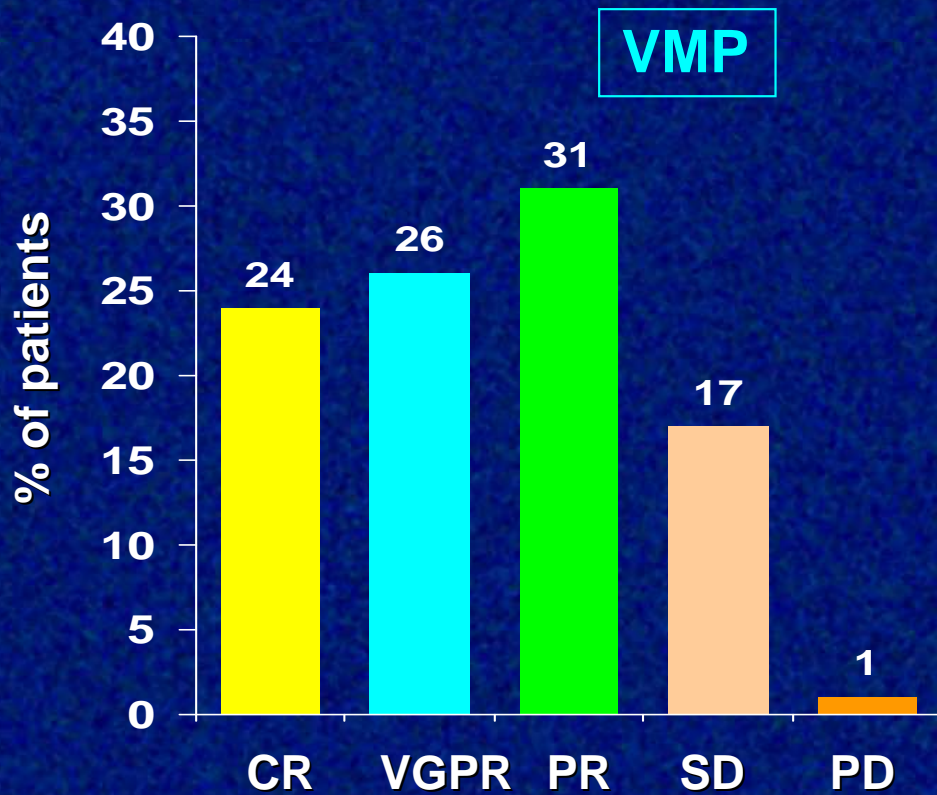
\* 66 VMP patients and 73 VMPT patients were treated with twice weekly infusions of Bortezomib

# Patient Characteristics

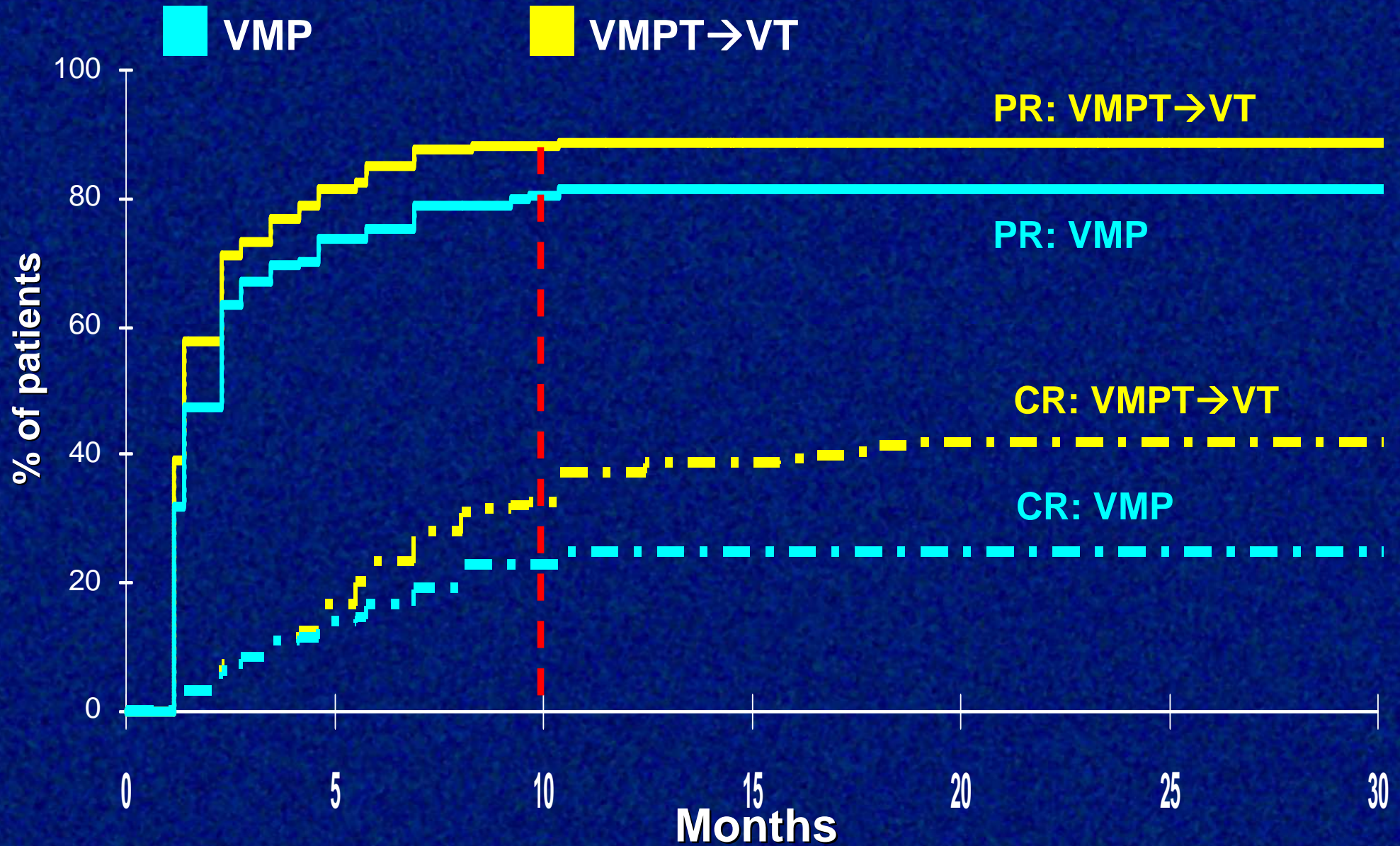
	VMP (N=257)	VMPT→VT (N=254)
Age (median)	71	71
< 65 years	2%	5%
65–74 years	71%	68%
≥ 75 years	27%	27%
β2 microglobulin-mg/L (median)	4	3.8
Chromosome abnormalities		
t(4;14)	14%	17%
t(14;16)	3%	5%
Del 17	13%	17%

# Best response

	VMP (N=253)	VMPT→VT (N=250)	P value
CR	24%	38%	0.0008
≥ VGPR	50%	59%	0.03
≥ PR	81%	89%	0.01



# Time to first response

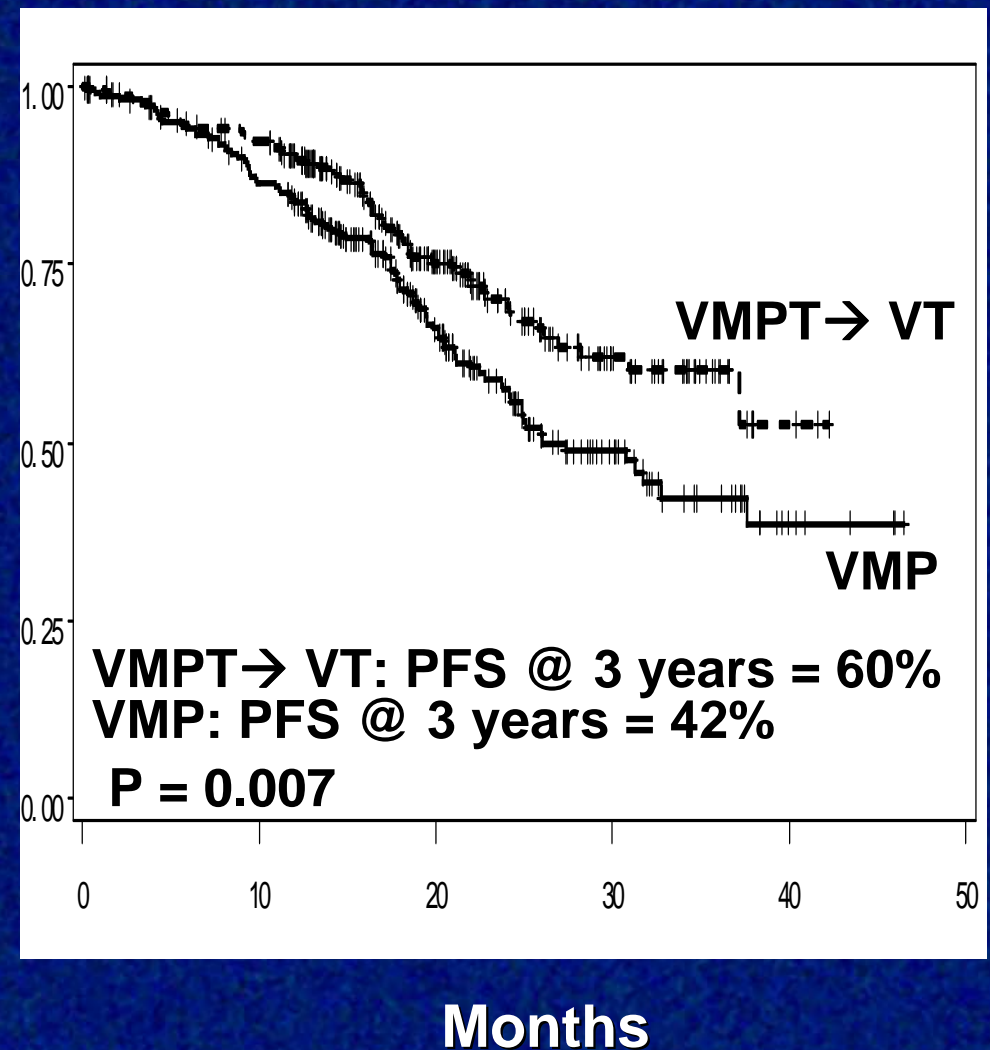
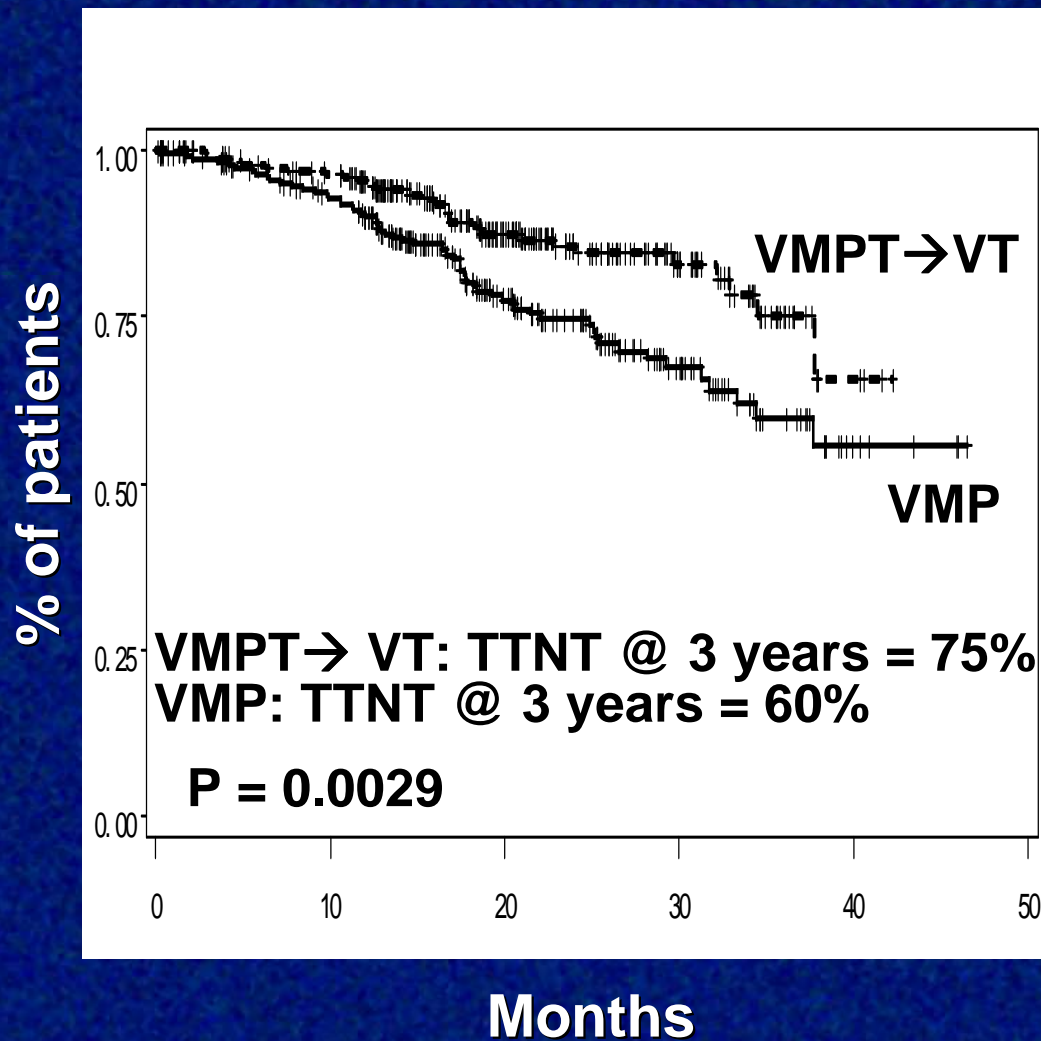


# Time to next therapy Progression free survival

Median follow-up 21.6 months

Time to next therapy

Progression free survival

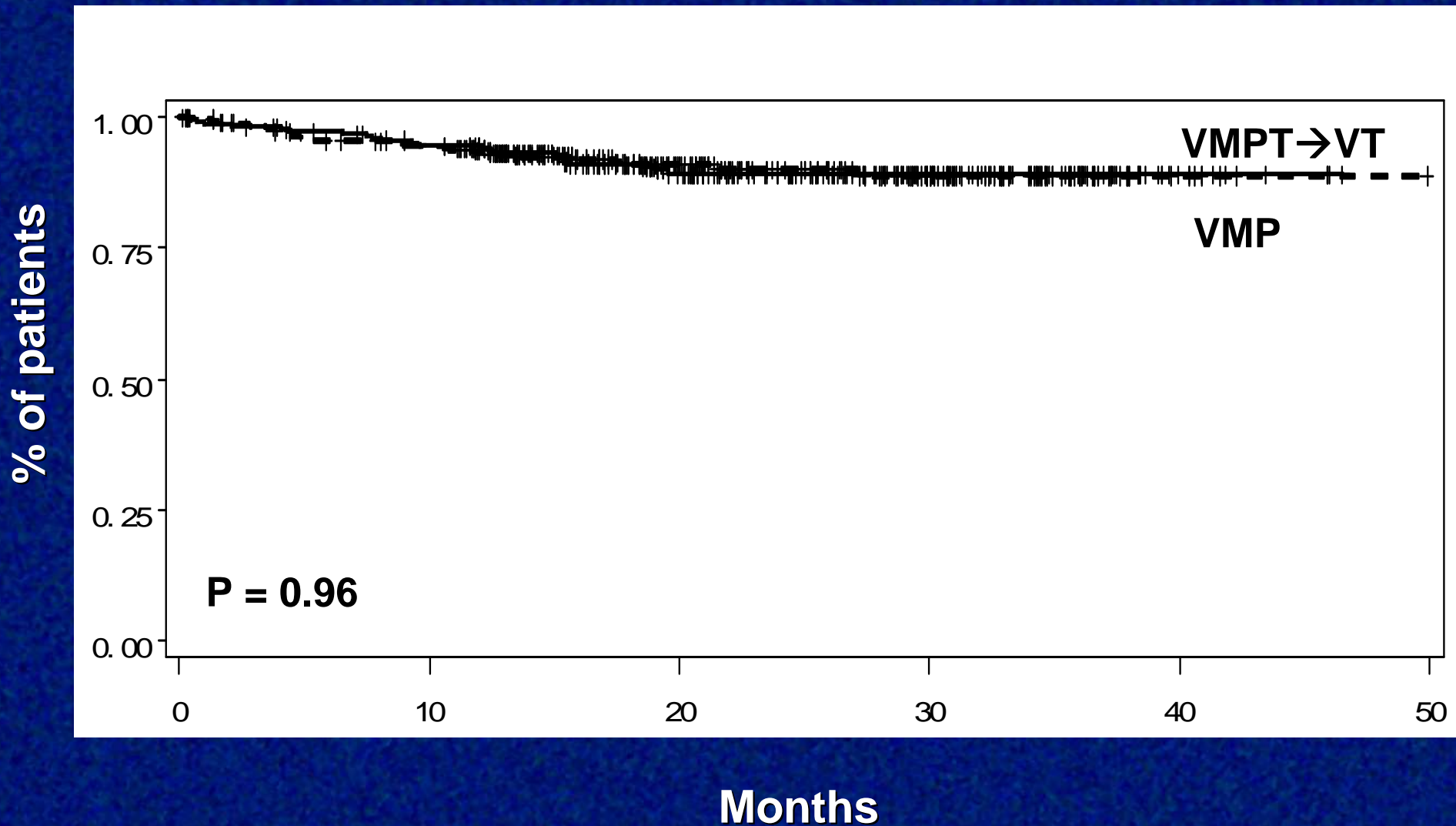




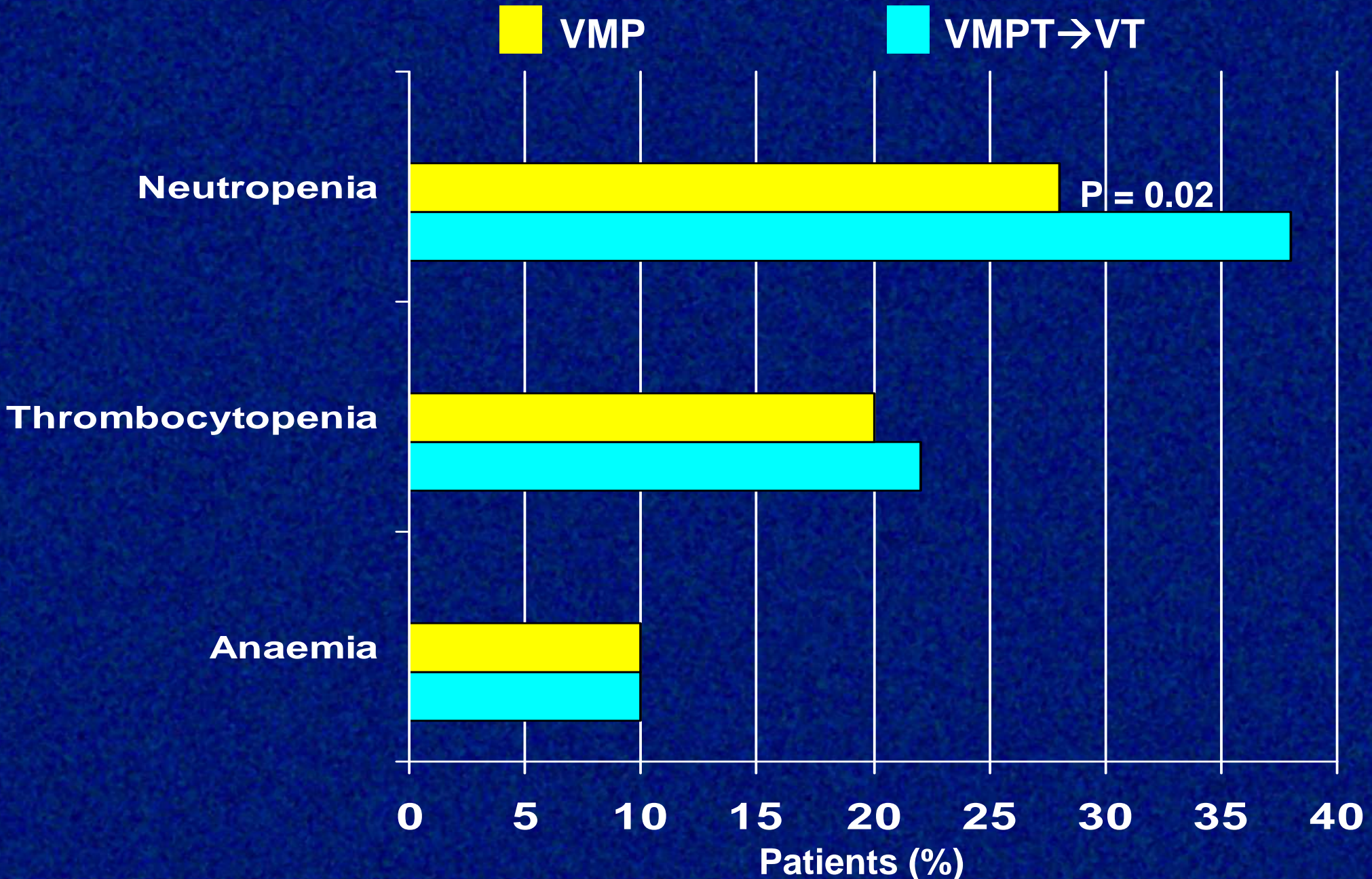
# Overall survival

VMPT→VT: OS @ 3 years = 89.2%

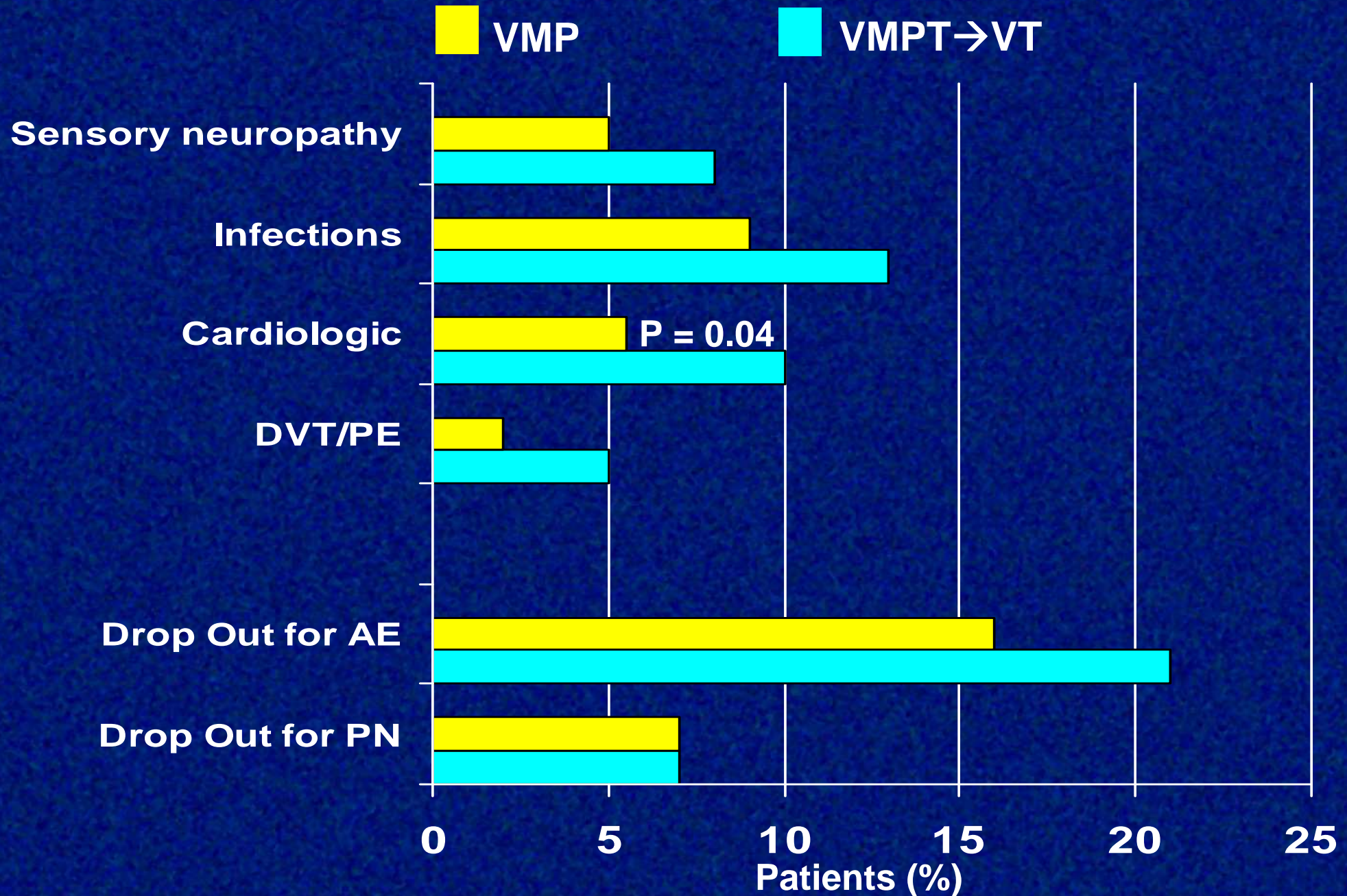
VMP: OS @ 3 years = 88.8%



# Grade 3-4 Hematologic Adverse Events



# Grade 3-4 Non-hematologic Adverse Events



# Efficacy and Toxicity by Bortezomib schedule

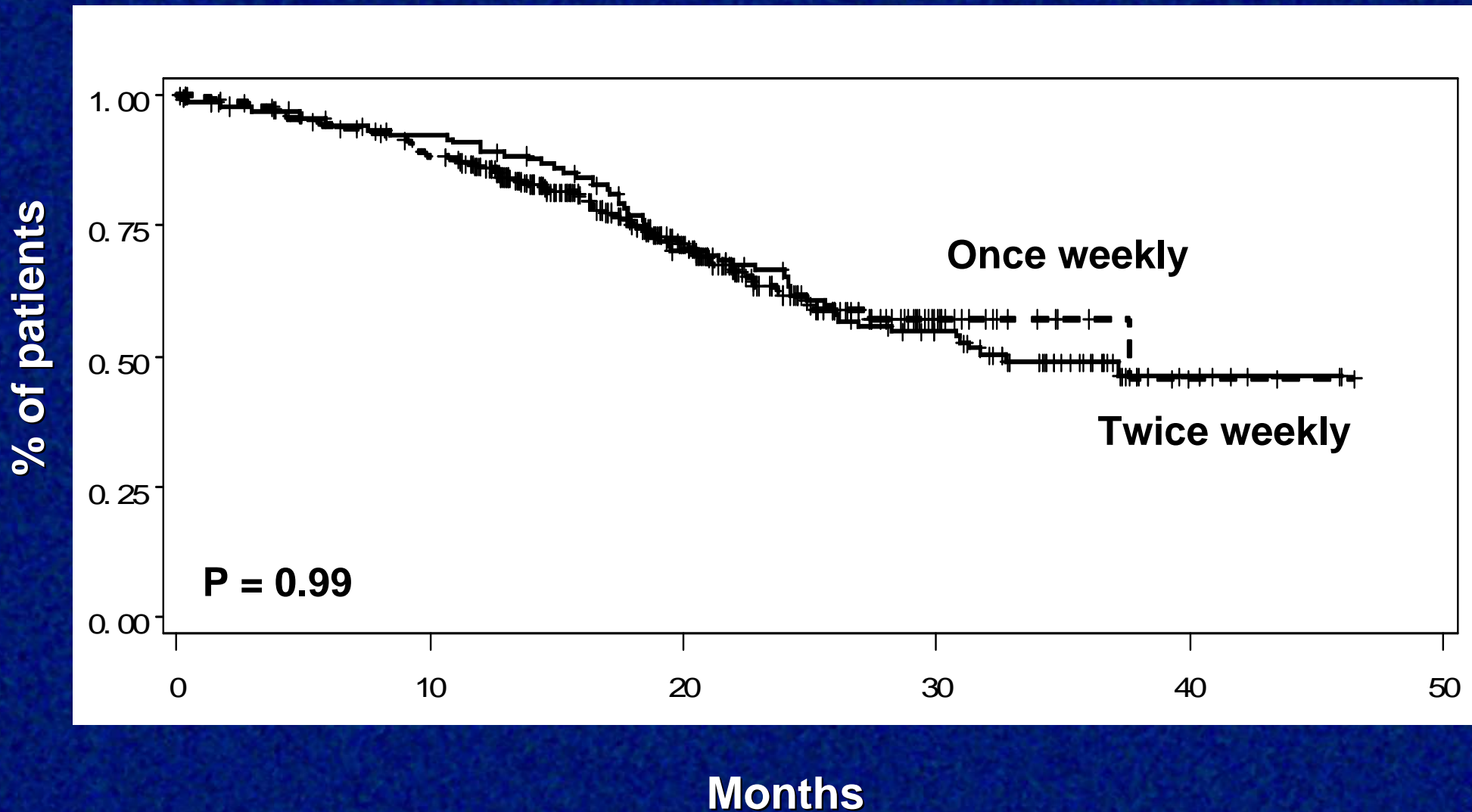
	<b>VMP* (VISTA)</b>	<b>VMP twice weekly N=63</b>	<b>VMP once weekly N=190</b>
<b>CR</b>	<b>30%</b>	<b>25%</b>	<b>23%</b>
<b>PFS @ 2 years</b>	<b>48%</b>	<b>56%</b>	<b>58%</b>
<b>Sensory PN</b>			
<b>Any grade</b>	<b>44%</b>	<b>43%</b>	<b>21%</b>
<b>Grade 3-4</b>	<b>13%</b>	<b>14%</b>	<b>2%</b>
<b>PN discontinuation</b>	<b>NA</b>	<b>16%</b>	<b>4%</b>
<b>Total planned dose</b>	<b>67.6</b>	<b>67.6 mg/m<sup>2</sup></b>	<b>46.8 mg/m<sup>2</sup></b>
<b>Total delivered dose</b>	<b>NA</b>	<b>41 mg/m<sup>2</sup></b>	<b>40 mg/m<sup>2</sup></b>

\*San Miguel JF et al. New Eng J Med 2008; 359: 906-17;  
 PN: peripheral neuropathy

# PFS according to Bortezomib schedule

Twice weekly: PFS @ 2 years = 61%

Once weekly: PFS @ 2 years = 62%

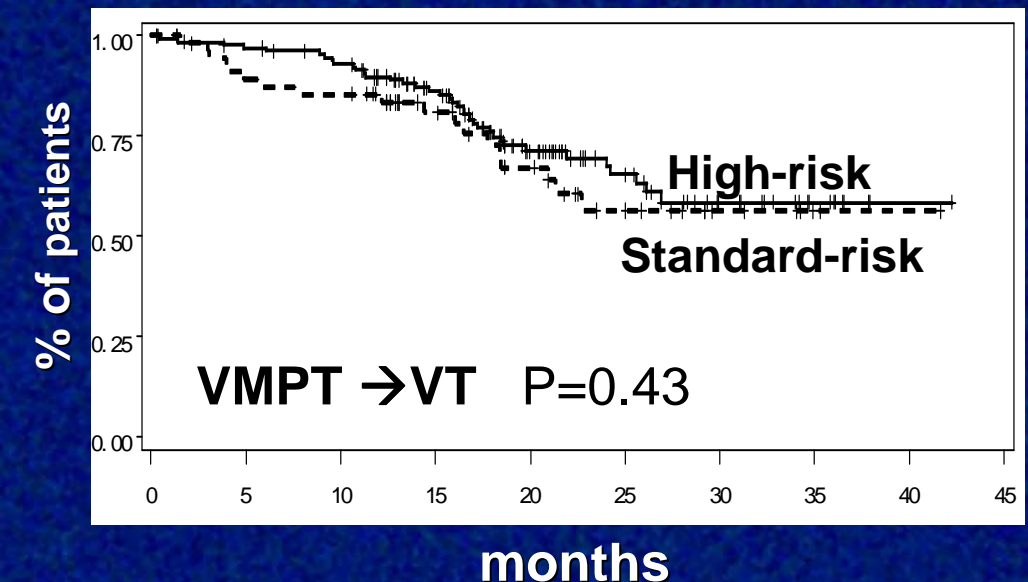
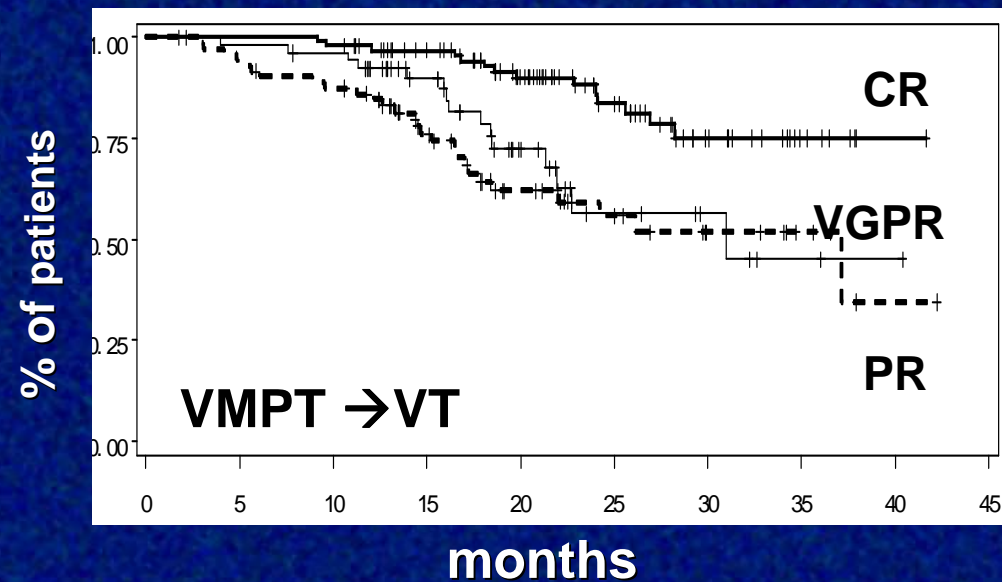
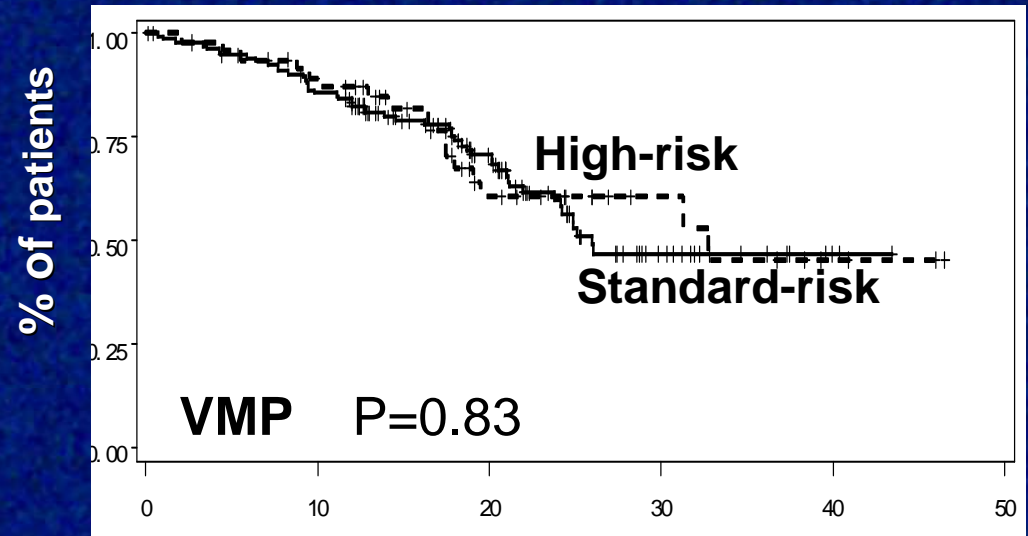
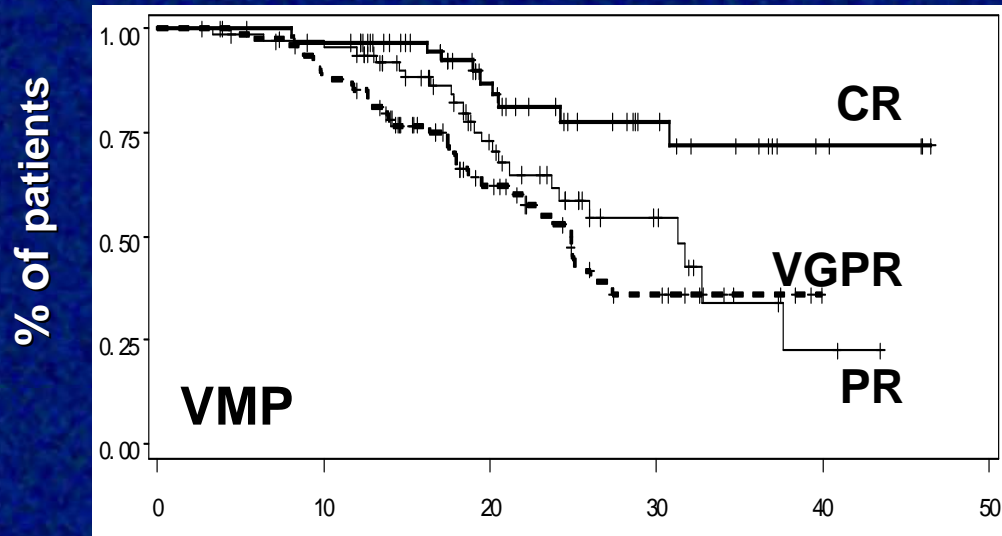


# PFS: VMP and VMPT→VT

according to response and chromosome abnormalities

## CR vs VGPR vs PR

## t(4;14) or t(14;16) or del17



# Conclusions 1

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	<b>VMP (N=253)</b>	<b>VMPT→VT (N=250)</b>	<b>P value</b>
<b>CR</b>	<b>24%</b>	<b>38%</b>	<b>0.0008</b>
<b>TTNT @ 3 years</b>	<b>60%</b>	<b>75%</b>	<b>0.0029</b>
<b>PFS @ 3 years</b>	<b>42%</b>	<b>60%</b>	<b>0.007</b>
<b>OS @ 3 years</b>	<b>89%</b>	<b>89%</b>	<b>0.96</b>

## Conclusions 2

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- VMPT → VT improves response rate and PFS
  - VMPT increases CR rate
  - VT maintenance improves PFS
- Longer follow-up is needed to assess OS
- Weekly infusion of bortezomib reduces peripheral neuropathy



# 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
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