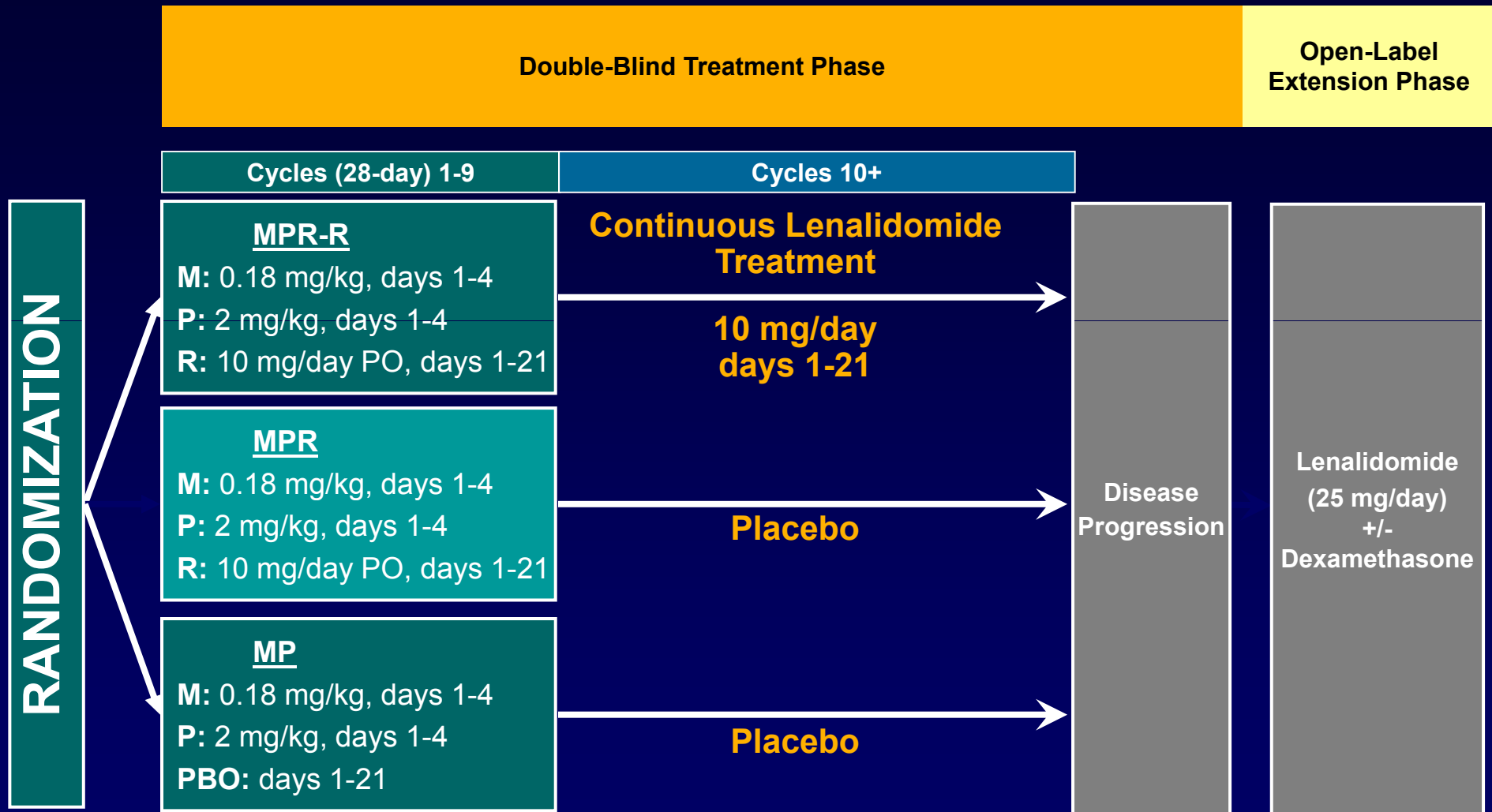


A Phase III Study to Determine the Efficacy and Safety of Lenalidomide Combined with Melphalan and Prednisone in Patients \geq 65 Years With Newly Diagnosed Multiple Myeloma (NDMM)

Antonio Palumbo, Meletios Dimopoulos, Michel Delforge, Roman Hajek, Martin Kropff, Maria Teresa Petrucci, Zhinuan Yu, Lindsay Herbein, Jay Mei, Christian Jacques, John Catalano

Phase III Study Schema

N = 459, 82 centers in Europe, Australia, and Israel



Stratified by age (≤ 75 vs > 75 years) and stage (ISS I/II vs III)

M, melphalan; P, prednisone; R, lenalidomide; PBO, placebo; po, orally; ISS, International Staging System.

Palumbo A, et al. *Haematologica*. 2010;95(suppl 1): Abstract 0566.

Patient Characteristics

	MPR-R N = 152	MPR N = 153	MP N = 154
Median age, years (range)	71 (65-87)	71 (65-86)	72 (65-91)
65 - 75 years of age, %	76	76	75
BM plasma cells, %	35	39	35
Cr _{CL} <60 mL/min, %	51	45	49
ISS Stage I / II / III, %	18 / 33 / 49	21 / 31 / 48	18 / 31 / 51

BM, bone marrow; Cr_{CL}, creatinine clearance; ISS, International Staging System.

Updated Follow-Up

- **First interim analysis at 50% of events (ASH 2009)**
- **Second interim analysis at 70% of events**
 - Data cut-off December 1, 2009
 - No patient unblinded
- **Median follow-up: 21 months**
- **Central adjudication committee reviewed efficacy data**

Best Response Rate

Best overall response ^a	MPR-R N = 152	MPR N = 153	MP N = 154	P Value (MPR-R vs MP)
ORR (≥PR), %	77	68	50	<.001
CR ^b , %	16	11	4	<.001
≥VGPR ^c , %	32	33	12	<.001
PR, %	45	35	38	—
SD, %	18	26	46	—
Median time to first response, months	2	2	3	<.001

^a As measured using EBMT criteria (Bladé J, et al. *Br J Haematol.* 1998;102(5):1115-1123)

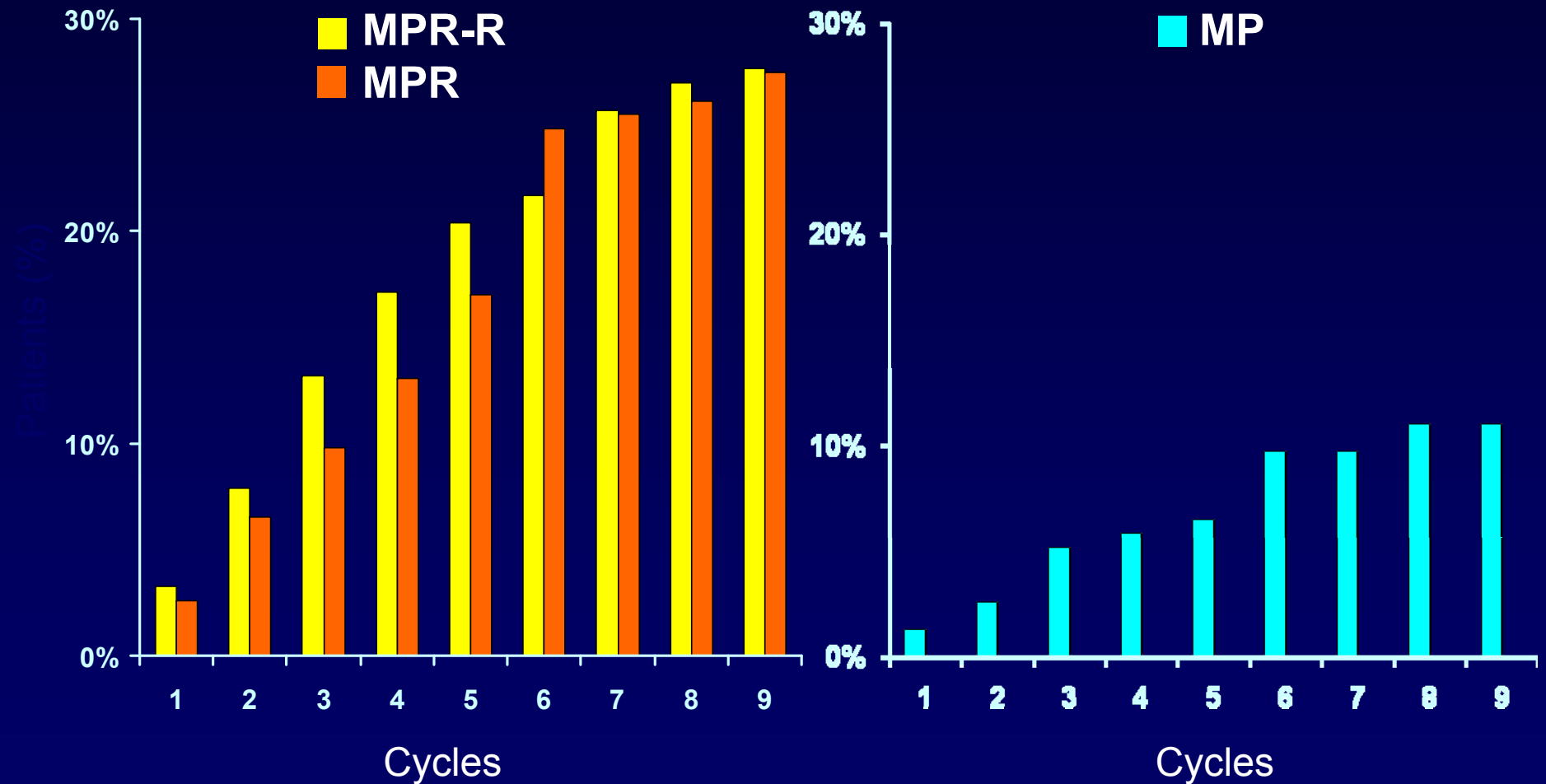
^b Immunofixation negative with or without bone marrow confirmation

^c VGPR: >90% reduction in M-protein

ORR, overall response rate; CR, complete response; VGPR, very good partial response; PR, partial response; SD, stable disease

Palumbo A, et al. *Haematologica.* 2010;95(suppl 1): Abstract 0566.

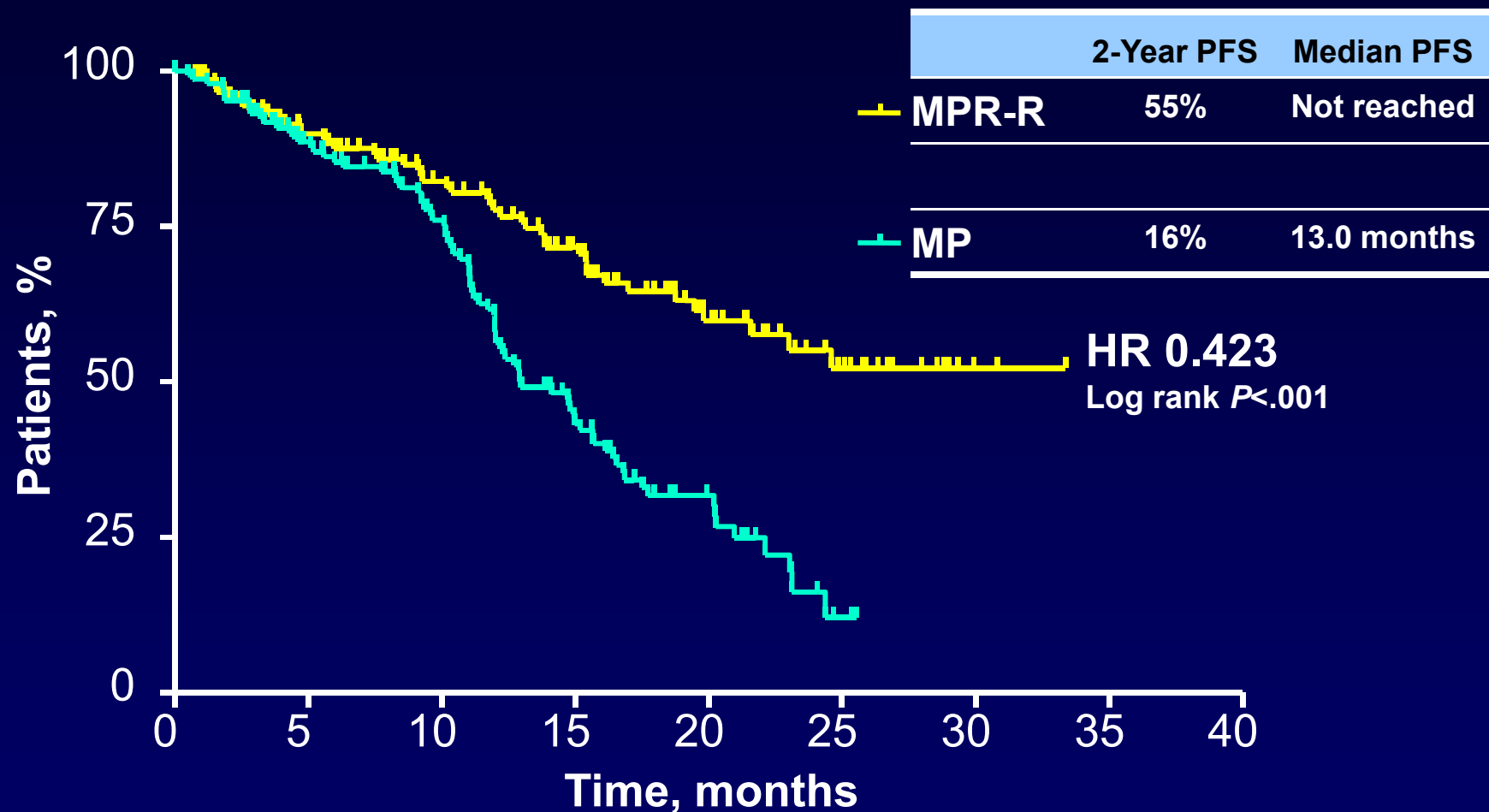
Response Improves Over Time ≥VGPR in All Patients



Palumbo A, et al. *Haematologica*. 2010;95(suppl 1): Abstract 0566.

Progression-Free Survival

58% Reduced Risk of Progression

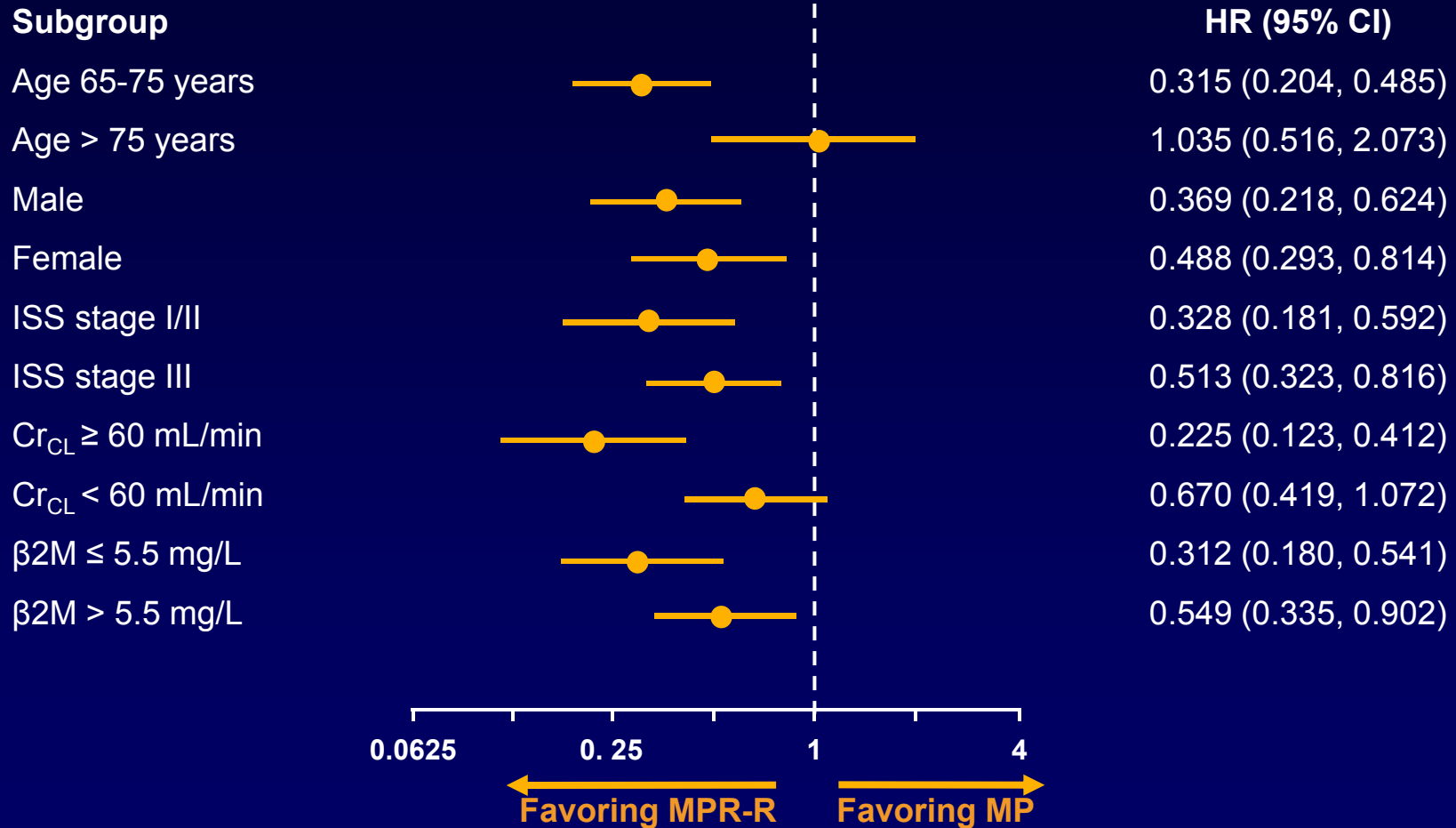


No. at Risk

MPR-R	152	115	89	66	35	17	2	—	—
MP	154	112	85	43	19	2	—	—	—

Palumbo A, et al. *Haematologica*. 2010;95(suppl 1): Abstract 0566.

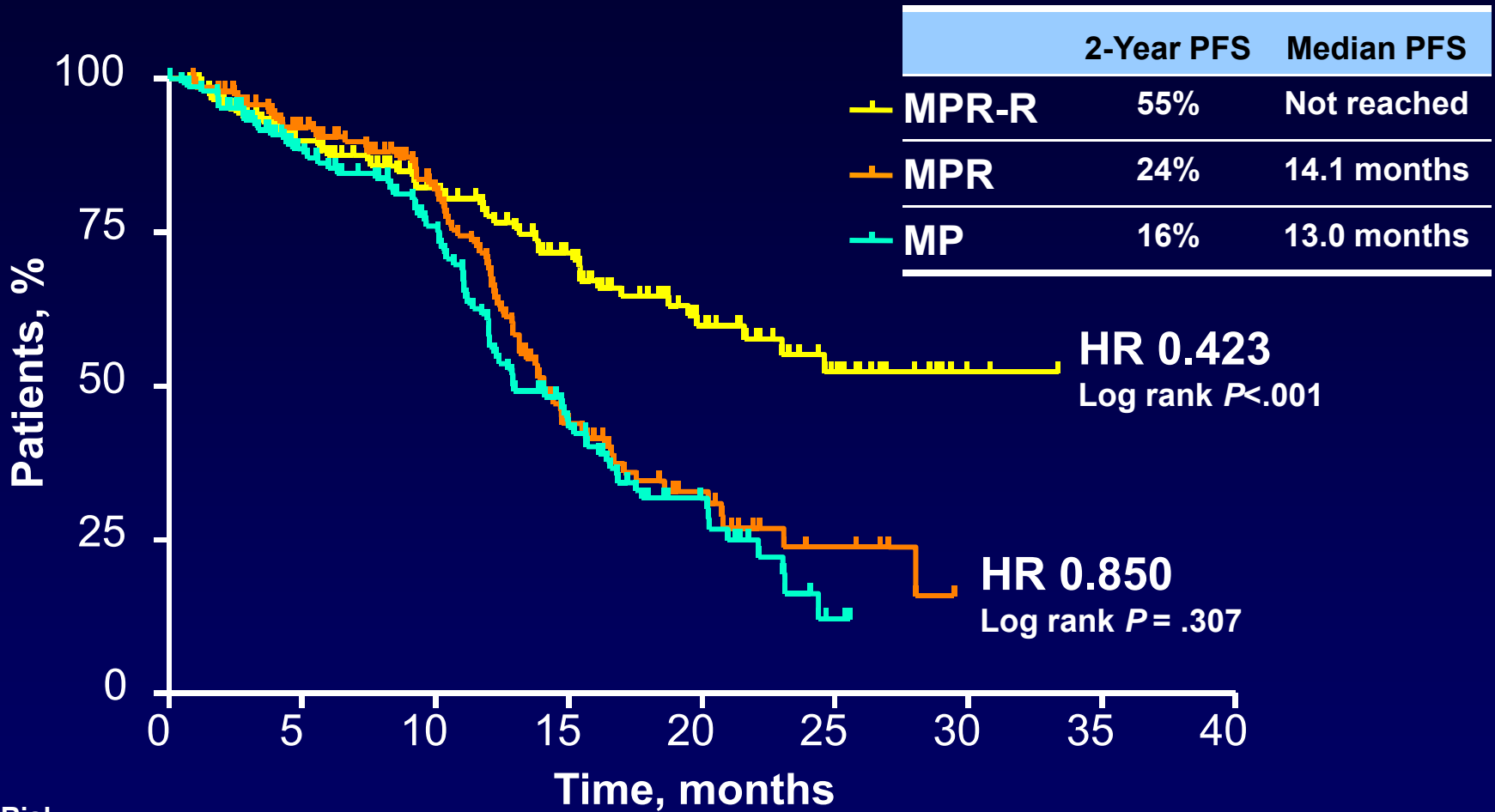
PFS Hazard Ratios by Subgroups MPR-R vs MP



ISS, International Staging System; Cr_{CL}, Creatinine Clearance; β2M, beta 2 microglobulin.

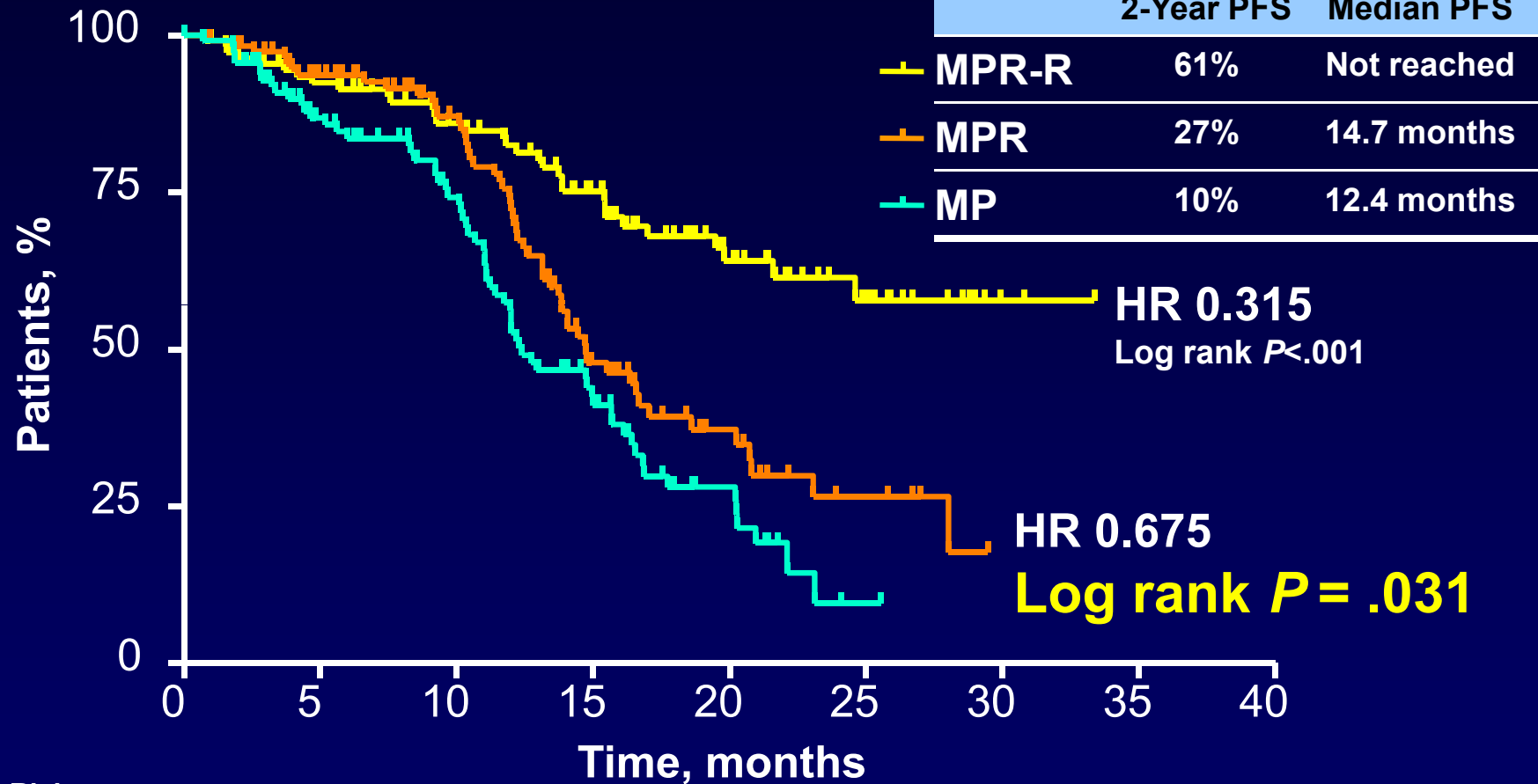
Palumbo A, et al. *Haematologica*. 2010;95(suppl 1): Abstract 0566.

Progression-Free Survival All Patients



No. at Risk											
MPR-R	152	115	89	66	35	17	2	—	—		
MPR	153	120	90	36	17	7	—	—	—		
MP	154	112	85	43	19	2	—	—	—		

Progression-Free Survival 65 - 75 Years of Age



No. at Risk									
MPR-R	116	91	75	57	31	15	2	—	—
MPR	116	97	77	31	16	7	—	—	—
MP	116	82	62	29	13	1	—	—	—

Treatment – Initial 9 cycles

	MPR ^a	MP
Discontinuation rate^b, %		
65 - 75 years of age	17	10
> 75 years of age	34	16
Cumulative dose intensity^c, %		
65 - 75 years of age	88	97
> 75 years of age	56	97

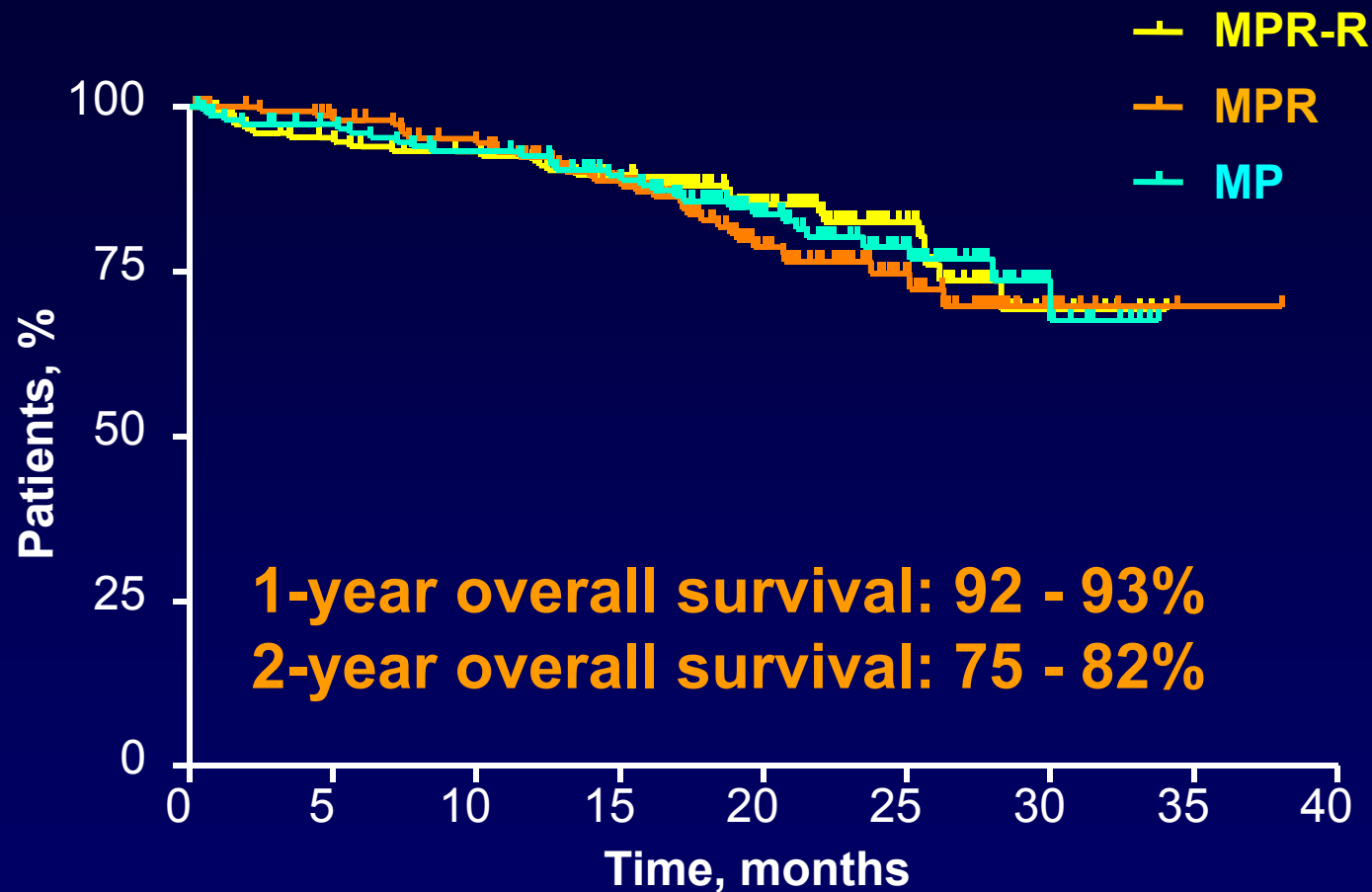
^a MPR includes MPR-R and MPR for the initial 9 cycles.

^b Discontinuation due to AEs or withdrawal of consent

^c Cumulative dose intensity of melphalan and lenalidomide/placebo

Palumbo A, et al. *Haematologica*. 2010;95(suppl 1): Abstract 0566.

Overall Survival



- Small number of events, median follow-up of 21 months

Grade 3/4 Adverse Events

Adverse events, %	MPR-R		MP	
	Grade 3	Grade 4	Grade 3	Grade 4
Anemia	21	3	16	1
Thrombocytopenia	25	13	10	4
Neutropenia	35	36	22	8
Febrile neutropenia	5	2	0	0
Infections	9	1	8	0
Fatigue	5	0	3	0
Rash	4	0	1	0
DVT/PE	2	1	1	0
Peripheral neuropathy	0	0	0	0

- G-CSF administration (66% MPR-R vs 31% MP)
- Platelet transfusion (35% MPR-R vs 18% MP)
- Overall discontinuation due to AEs (20% MPR-R vs 8% MP)

DVT, deep vein thrombosis; PE, pulmonary embolism.

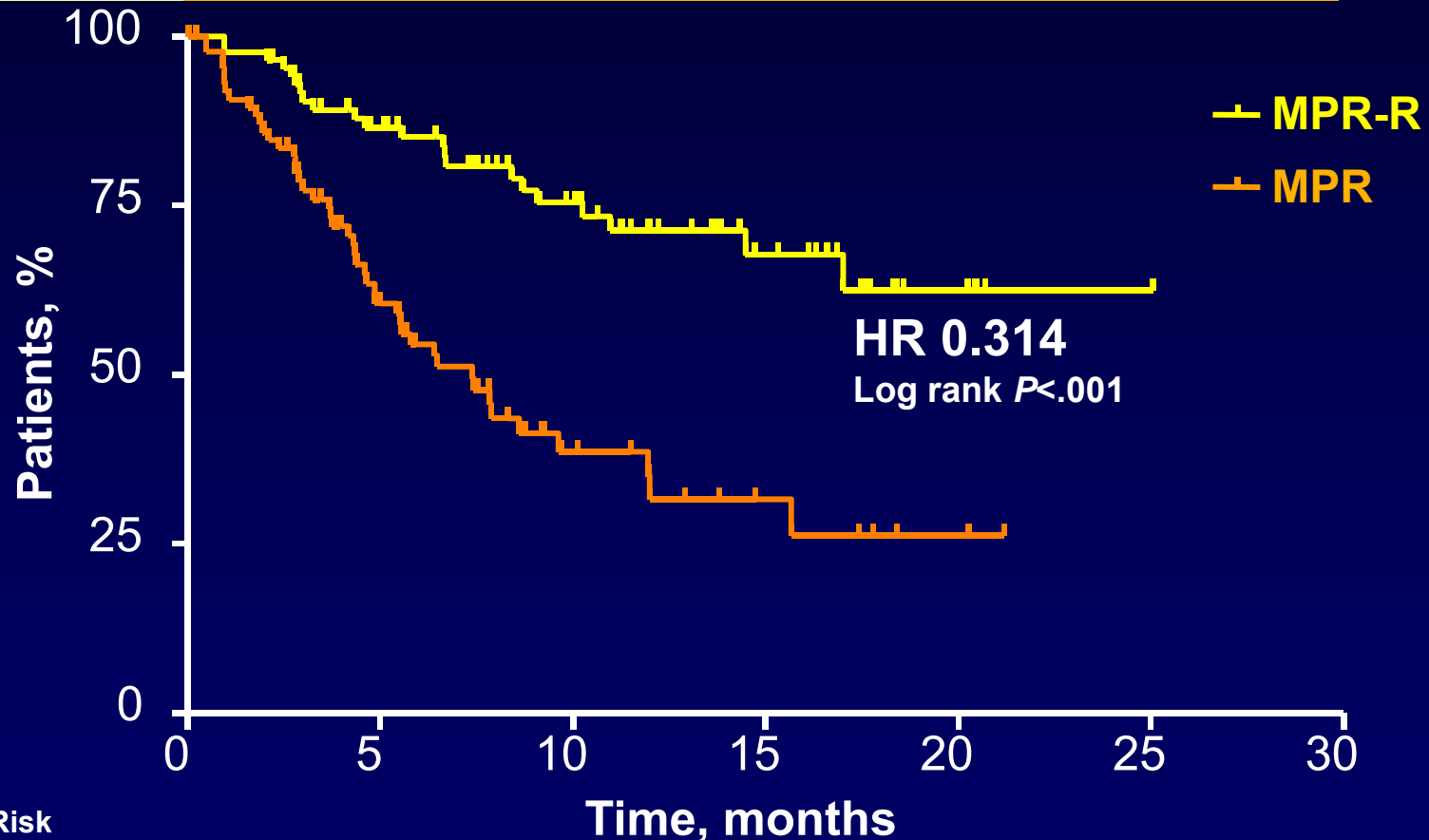
Palumbo A, et al. *Haematologica*. 2010;95(suppl 1): Abstract 0566.

Landmark Analysis

69% Reduced Risk of Progression

MPR

Lenalidomide Continuous Therapy



No. at Risk	0	5	10	15	20	25	30
MPR-R	88	66	40	18	5	1	—
MPR	94	41	13	6	2	—	—

Palumbo A, et al. *Haematologica*. 2010;95(suppl 1): Abstract 0566.

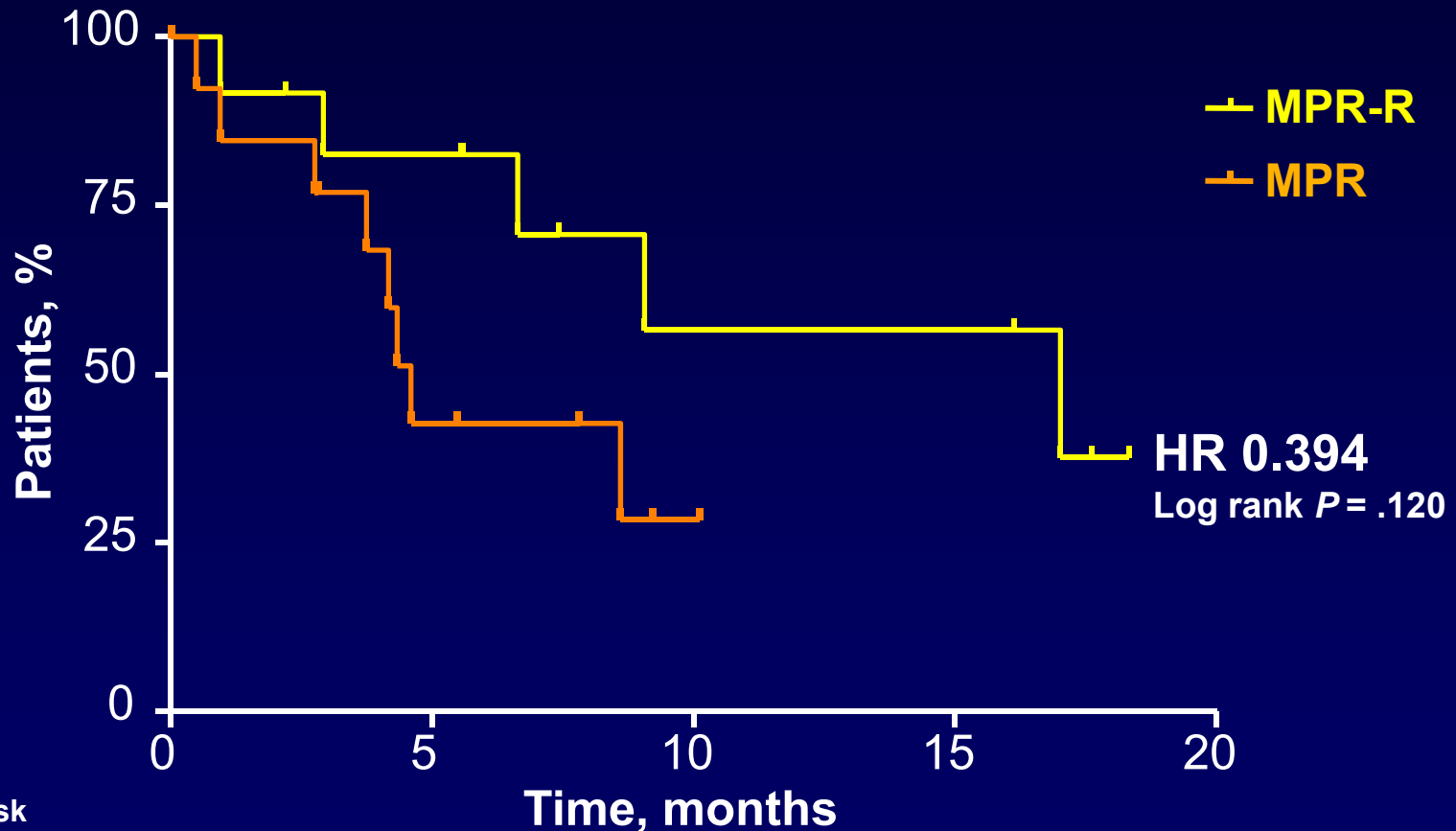
Landmark Analysis

> 75 Years of Age

61% Reduced Risk of Progression

MPR

Lenalidomide Continuous Therapy



No. at Risk

	0	5	10	15	20
MPR-R	12	9	4	4	—
MPR	14	5	1	—	—

Grade 3/4 Adverse Events After Cycle 9 Lenalidomide Continuous Therapy vs Placebo

Adverse Events ^a , %	Lenalidomide Continuous ^b N = 75	Placebo ^c N = 94
Anemia	0	5
Thrombocytopenia	3	2
Neutropenia	2	0
DVT	2	0
Rash	1	0
Fatigue	1	0
Peripheral neuropathy	0	1

^a Newly occurring or worsening Grade 3/4 adverse events

^b MPR-R

^c MP

DVT, deep vein thrombosis.

Palumbo A, et al. *Haematologica*. 2010;95(suppl 1): Abstract 0566.

Conclusions

- **MPR-R is a new standard treatment option for non-transplant eligible patients**
- **MPR is a highly active combination regimen**
 - **Greatest benefit observed in patients aged 65 – 75 years**
- **Continuous lenalidomide therapy achieved an unprecedented reduction in the risk for progression in patients aged 65 years and older**

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

Dimopoulos	Greece	Gobbi	Italy	Ahlgren	Sweden
Adam	Czech Republic	Dmoszynska	Poland	Masliak	Ukraine
Kropff	Germany	Domnikova	Russia	Kaplan	Ukraine
Foa	Italy	Rossiev	Russia	Keting	Ukraine
Palumbo	Italy	Cagirgan	Turkey	Taylor	Australia
Catalano	Australia	Prince	Australia	Scudla	Czech Republic
Gisslinger	Austria	Horvath	Australia	Jaccard	France
Jedrzejczak	Poland	Spencer	Australia	Morra-Barbarano	Italy
Delforge	Belgium	Gregersen	Denmark	Rukavitsin	Russia
Zodelava	Georgia	Engelhardt	Germany	Capote	Spain
Weisel	Germany	Terpos	Greece	Zweegman	The Netherlands
Cascavilla	Italy	Rowe	Israel	Pilipenko	Ukraine
Van Droogenbroeck	Belgium	Hellmann	Poland	Lysaya	Ukraine
Iosava	Georgia	Abdulkadyrov	Russia	Tretyak	Ukraine
Cavo	Italy	Greil	Austria	Joshua	Australia
Kloczko	Poland	Maisnar	Czech Republic	Mollee	Australia
Blade Creixenti	Spain	Attal	France	Augustson	Australia
Beksac	Turkey	Knop	Germany	Gastl	Austria
Spicka	Czech Republic	Alegre Amor	Spain	Rossi	France
Plesner	Denmark	Yong	United Kingdom	Goldschmidt	Germany
Naumann-Radke	Germany	Iskrov	Belarus	Crotty	Ireland
Liebisch-Langer	Germany	Fillet	Belgium	Skotnicki	Poland
Ben-Yehuda	Israel	Schots	Belgium	Osmanov	Russia
Corso	Italy	Macro	France	San Miguel	Spain
Ludwig	Austria	Dölken	Germany	Ríos Herranz	Spain
Niederwieser	Germany	Nagler	Israel	Stenner	Switzerland
Caravita	Italy	Shpilberg	Israel	Schey	United Kingdom
Uss	Belarus				

Best Response Rate

Best overall response ^a	MPR-R N = 152	MPR N = 153	MP N = 154	P Value (MPR-R vs MP)
ORR (≥PR), %	77	68	50	<.001
CR ^b , %	16	11	4	<.001
≥ VGPR ^c , %	32	33	12	<.001
PR, %	45	35	38	—
SD, %	18	26	46	—
Median time to first response, months	2	2	3	<.001
Median duration of response, months	NE	12.9	12.7	<.001

^a As measured using EBMT criteria (Bladé J, et al. *Br J Haematol.* 1998;102:1115-1123)

^b Immunofixation negative with or without bone marrow confirmation

^c VGPR: > 90% reduction in M-protein

ORR, overall response rate; CR, complete response; VGPR, very good partial response; PR, partial response; SD, stable disease

Palumbo A, et al. *Haematologica.* 2010;95(suppl 1): Abstract 0566.