Impact of Autologous Transplantation vs Chemotherapy Plus Lenolidomide in Newly Diagnosed Myeloma According to Patient Prognosis: Results of a Pooled Analysis of Two Phase II Trials

Abstract 198

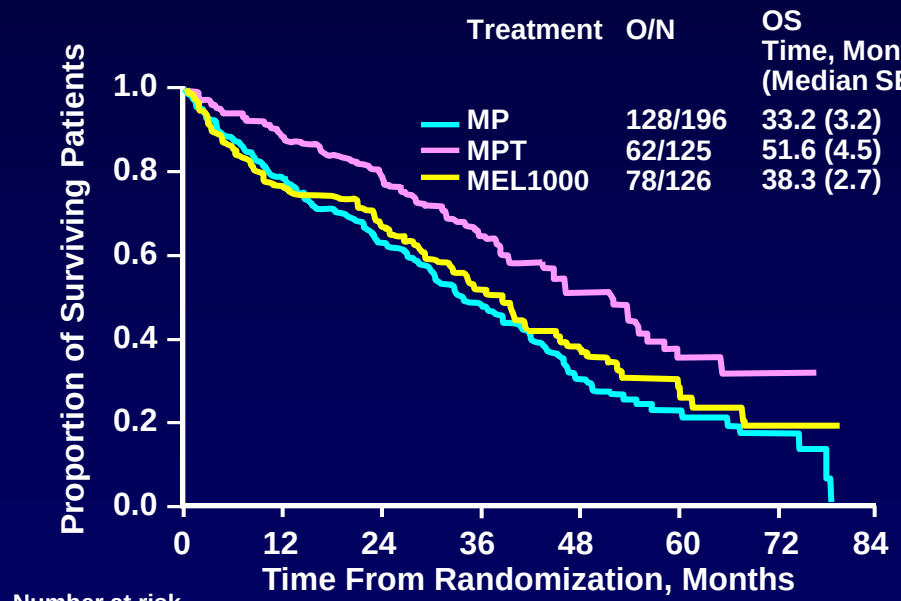
Gay F, Cerrato C, Hajek R, Di Raimondo F, Caravita T, Falcone AP, Patriarca F, Pulini S, Finsinger P, Ciccone G, Corradini P, Siniscalchi A, Donato F, Ben Yahuda D, Offidani M, Minarik J, Ria R, Cavallo F, Catalano L, Cavalli M, Pour L, Petrucci MT, Hardan I, Boccadoro M, Spencer A, Palumbo A

Rationale

ASCT vs Conventional Chemotherapy + Novel Agents

MPT vs Mel100-ASCT1

Age 65-75 years



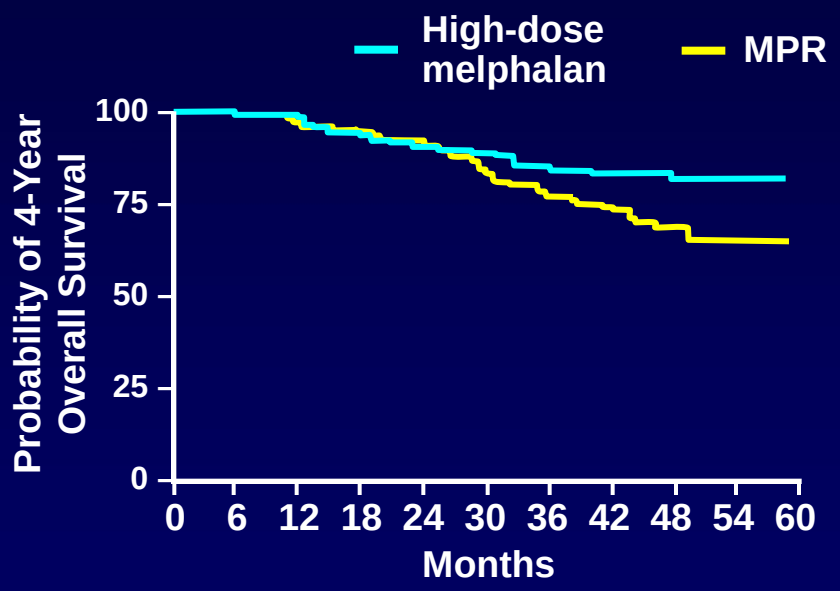
Number at risk

MP	196	170	153	136	111	85	67	49	30	24	13	10	6
MPT	125	117	109	104	90	78	58	47	38	26	16	9	3
MEL100	126	103	96	92	76	62	50	36	29	19	12	6	4

MPT vs Mel 100-ASCT: HR 0.59, *P* = .0006

MPR vs Mel200-ASCT[2]

Age ≤65 years



141	136	129	121	115	111	105	88	42	7
132	131	124	121	117	106	94	82	27	5

MPT200-ASCT vs MPR: HR 0.55, *P* = .02

MP, melphalan-prednisone; MPT, MP plus thalidomide; ASCT, autologous stem-cell transplantation; Mel100, melphalan 100 mg/m^2; MPR, melphalan-prednisone-lenalidomide

Gay F, et al. *Blood.* 2014;124: Abstract 198.

1. Facon T, et al. *Lancet.* 2007;370(9594):1209-1218.
2. Palumbo A, et al. *N Engl J Med.* 2014;371(10):895-905.

Aims

- To compare **Mel200-ASCT vs CC+R** in a large population of patients ≤65 years
  - PFS1
  - PFS2
  - OS

- To evaluate the role of **ASCT as salvage therapy** at first relapse

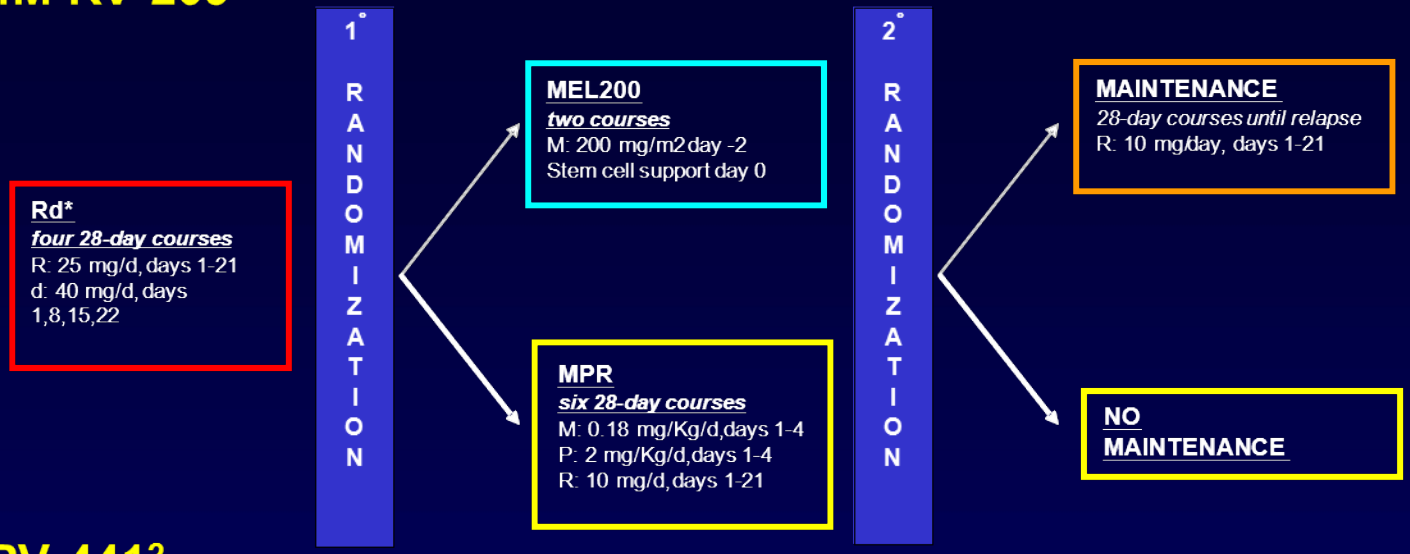
- To compare Mel200-ASCT vs CC+R in subgroups of patients with different prognosis

→Is there a **subset of patients who may benefit from a less intensive oral therapy upfront, and transplant at first relapse**?

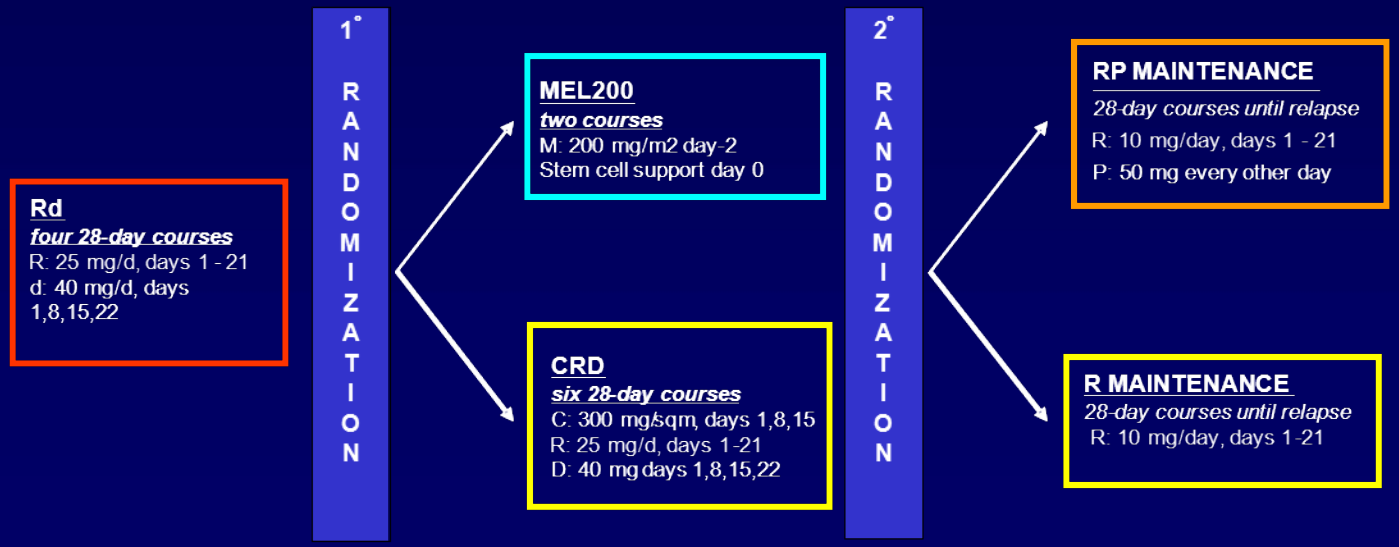
Gay F, et al. *Blood.* 2014;124: Abstract 198.

ASCT vs CC+Lenolidomide

GIMEMA MM-RV-209[1]



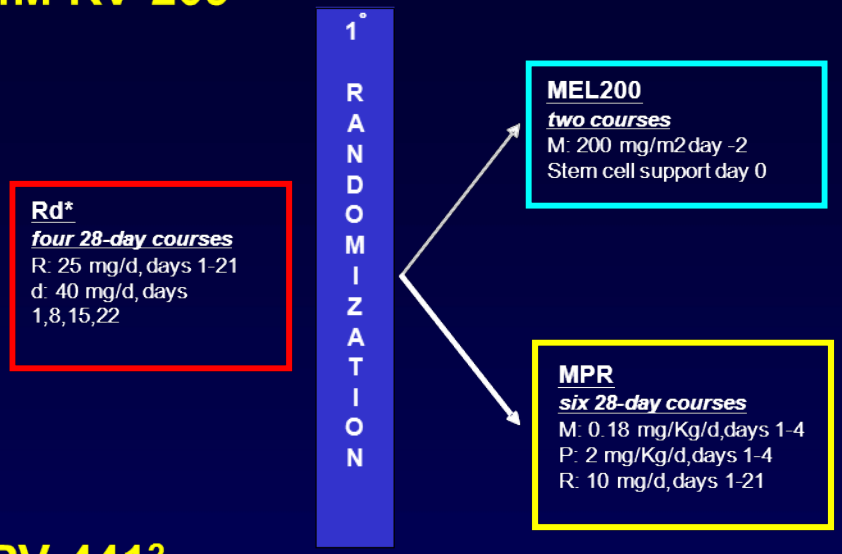
EMN MM-RV-441[2]



1. Palumbo A, et al. *N Engl J Med.* 2014;371(10):895-905; 2. Palumbo A, et al. *Blood.* 2013;122: Abstract 763.
Gay F, et al. *Blood.* 2014;124: Abstract 198.

ASCT vs CC+Lenolidomide

GIMEMA MM-RV-209[1]



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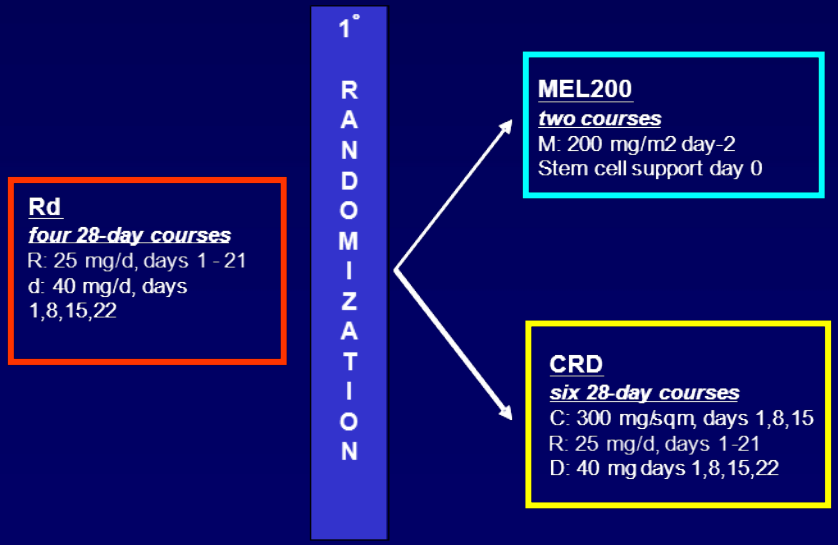

1. Palumbo A, et al. *N Engl J Med.* 2014;371(10):895-905; 2. Palumbo A, et al. *Blood.* 2013;122: Abstract 763.
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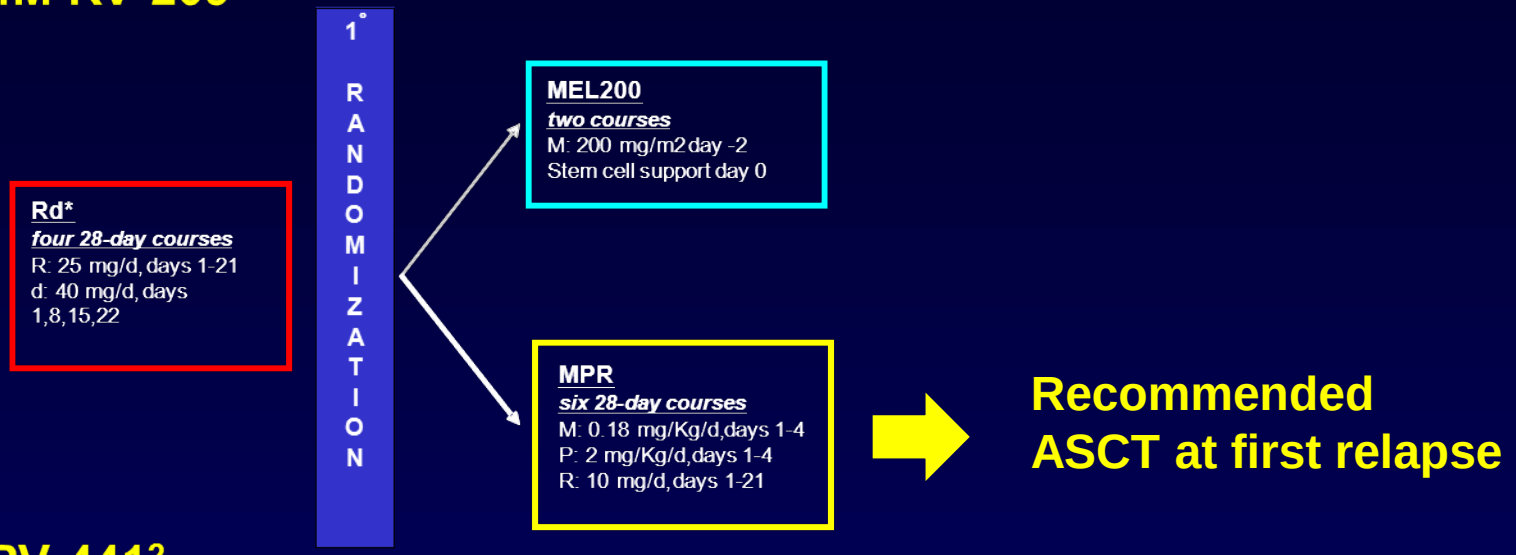
ASCT vs CC+Lenolidomide

GIMEMA MM-RV-209[1]



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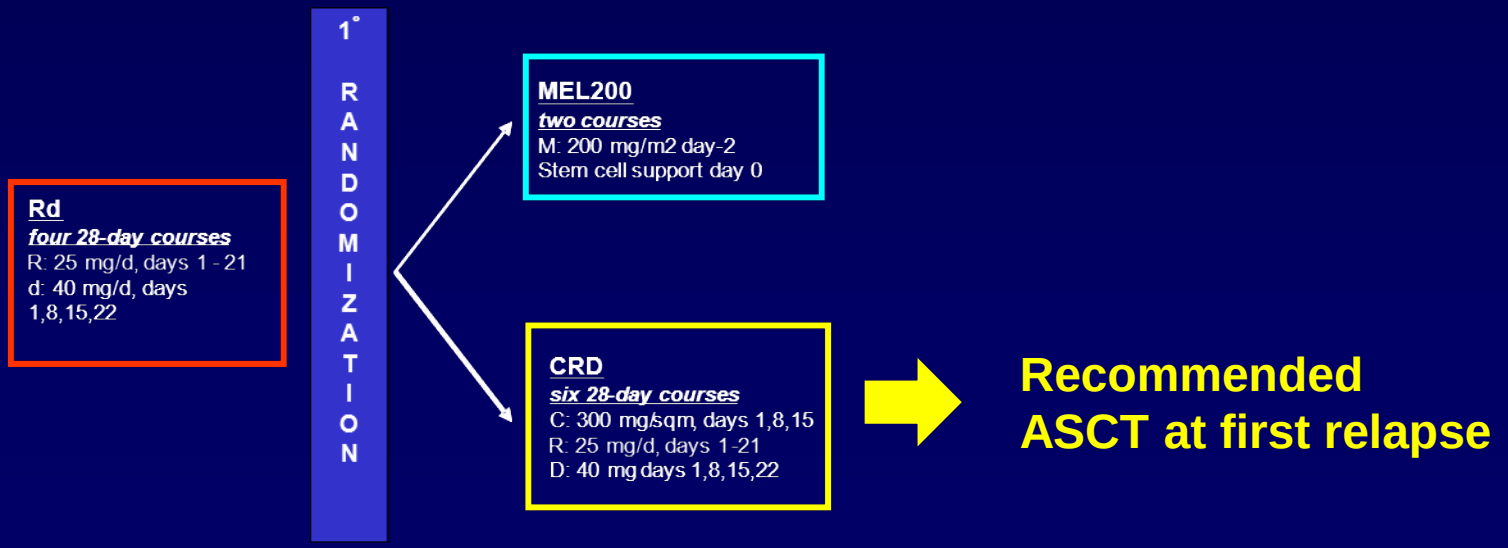

1. Palumbo A, et al. *N Engl J Med.* 2014;371(10):895-905; 2. Palumbo A, et al. *Blood.* 2013;122: Abstract 763.
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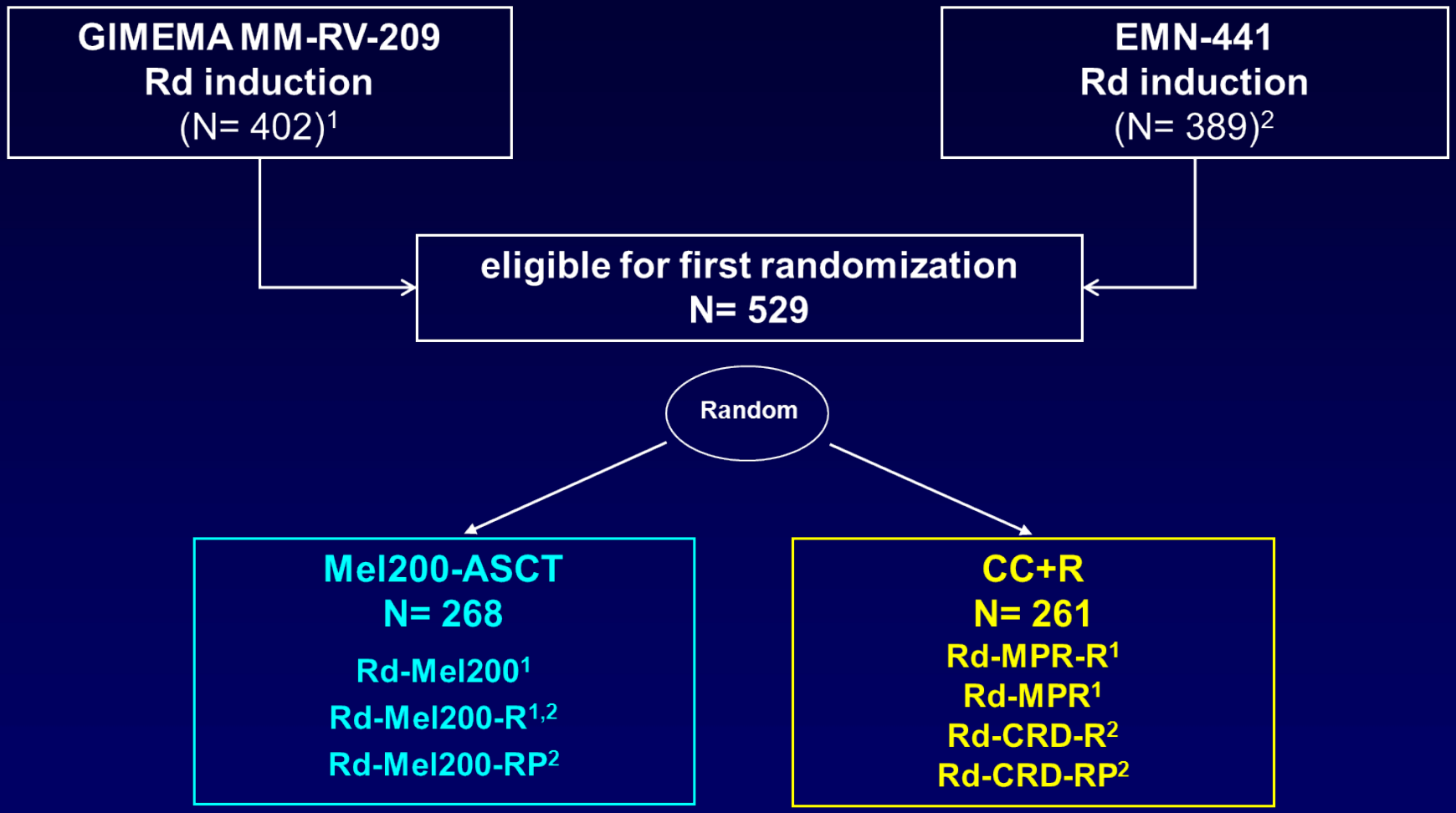
Study Design

• 2 phase III trials comparing Mel 200-ASCT vs CC+R



Mel200, melphalan 200 mg/m^2 followed by autologous stem-cell transplantation; CC+R, conventional therapy + lenalidomide; Rd, lenalidomide plus low-dose dexamethasone; MPR, melphalan-prednisone-lenalidomide; CRD, cyclophosphamide-lenalidomide-dexamethasone; RP, lenalidomide-prednisone maintenance, R, lenalidomide maintenance.

1. Palumbo A, et al. *N Engl J Med.* 2014;371(10):895-905; 2. Palumbo A, et al. *Blood.* 2013;122: Abstract 763.

Gay F, et al. *Blood.* 2014;124: Abstract 198.

Patient Characteristics

	Mel200-ASCT N = 268	CC+R N = 261
Age, median (IQR)	57 (52-62)	57 (51-61)
Male sex	52%	51%
ISS stage		
I	52%	47%
II	33%	33%
III	15%	20%
Cytogenetic Abnormalities Del 17 or t(4:14) or t(14:16)	19%	20%
Karnofsky performance score		
60%-70%	16%	13%
80%-100%	84%	87%
LDH ≥ULN	6%	8%
Response to induction		
≥VGPR	26%	31%
<VGPR	74%	69%

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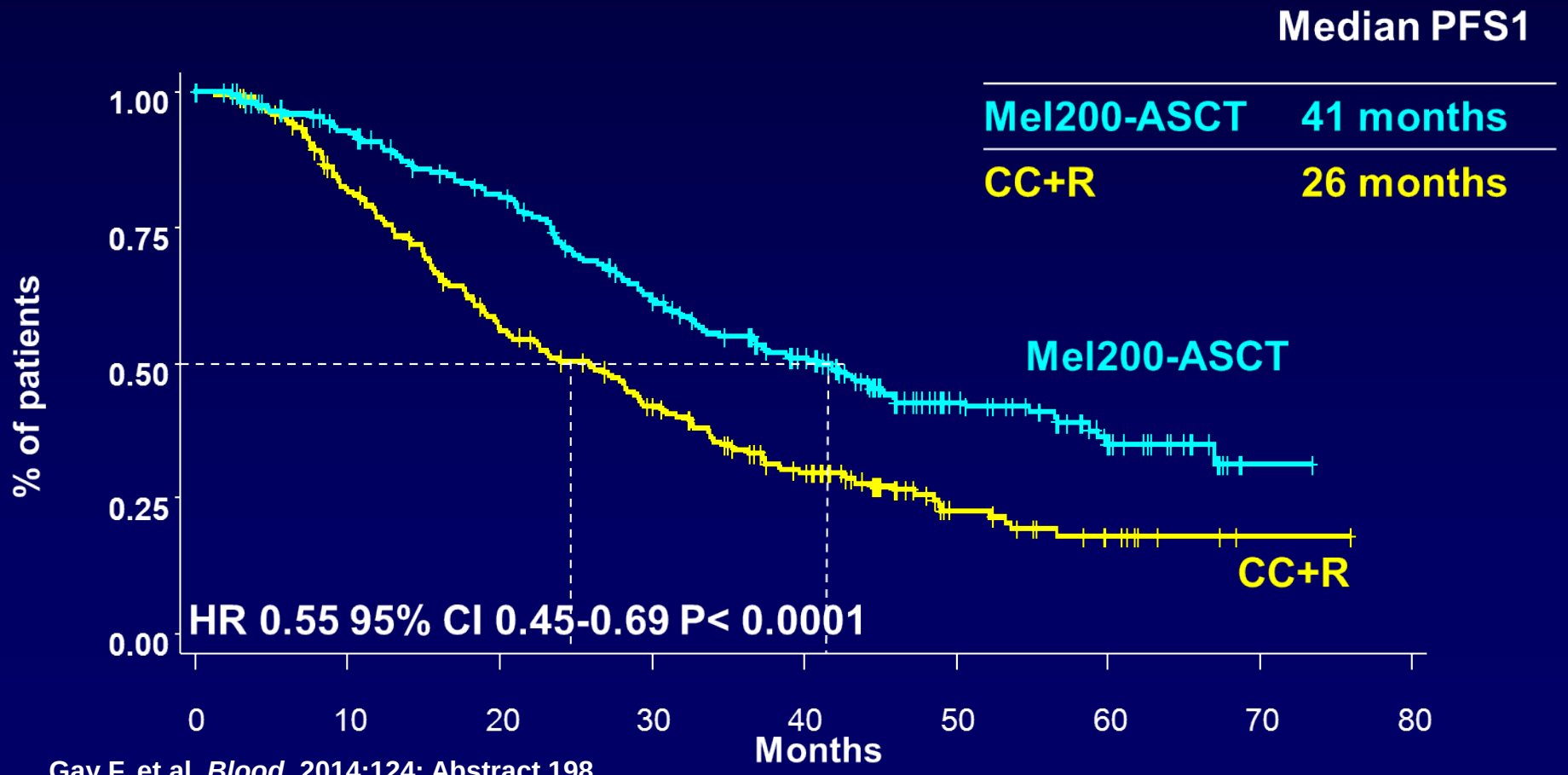
Mel200-ASCT vs CC+R: PFS1

Median follow-up from randomization: 4 years

PFS1: from random to first progression

First line	Second line	Subsequent lines	Death



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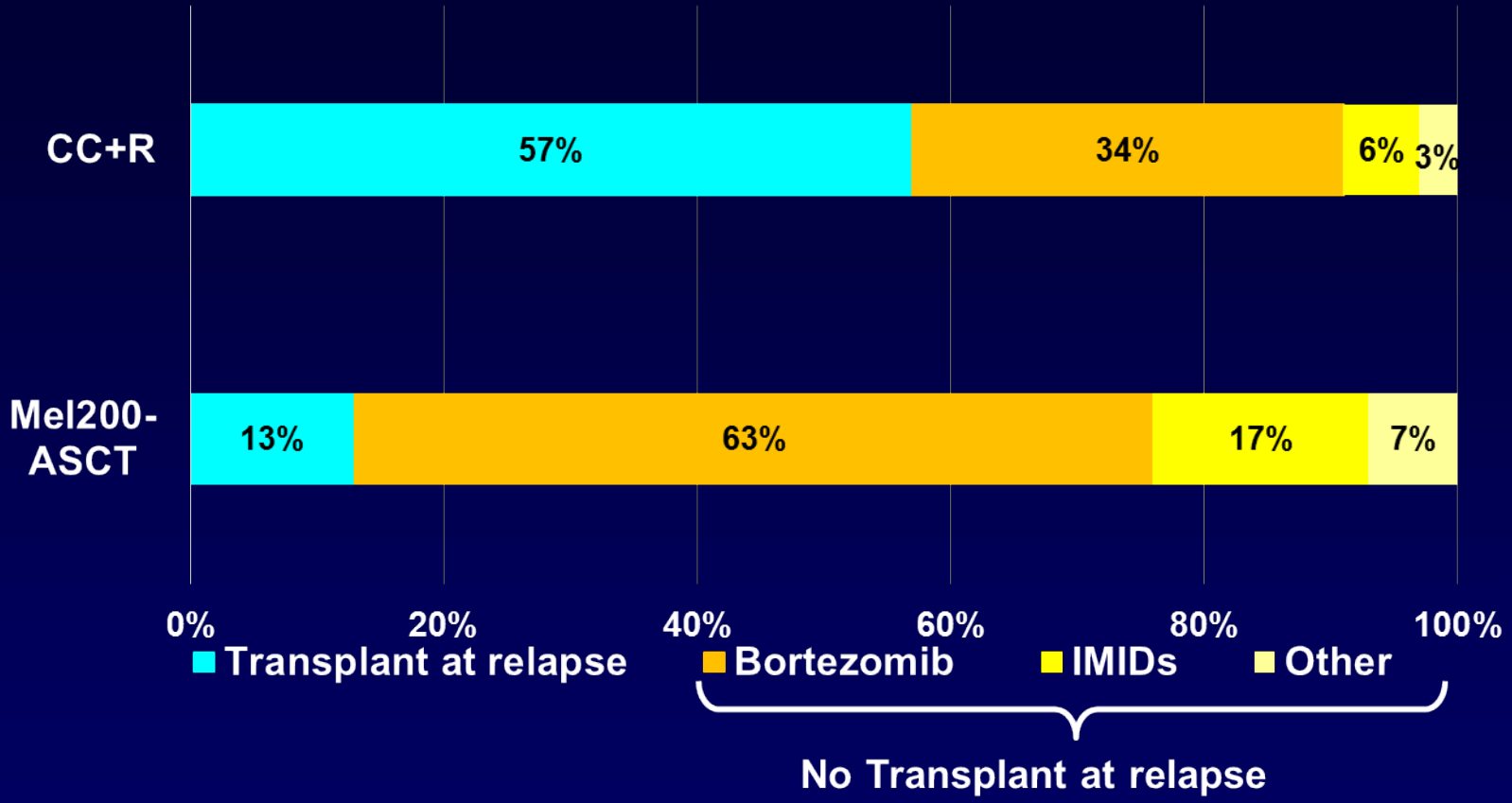
Mel200-ASCT vs CC+R: Second-Line Therapy



- Only 57% of patients relapsing from CC+R actually received ASCT
- Most of the patients who received ASCT at first relapse were reinduced with bortezomib (66% in Mel200-ASCT and 84% in CC+R)

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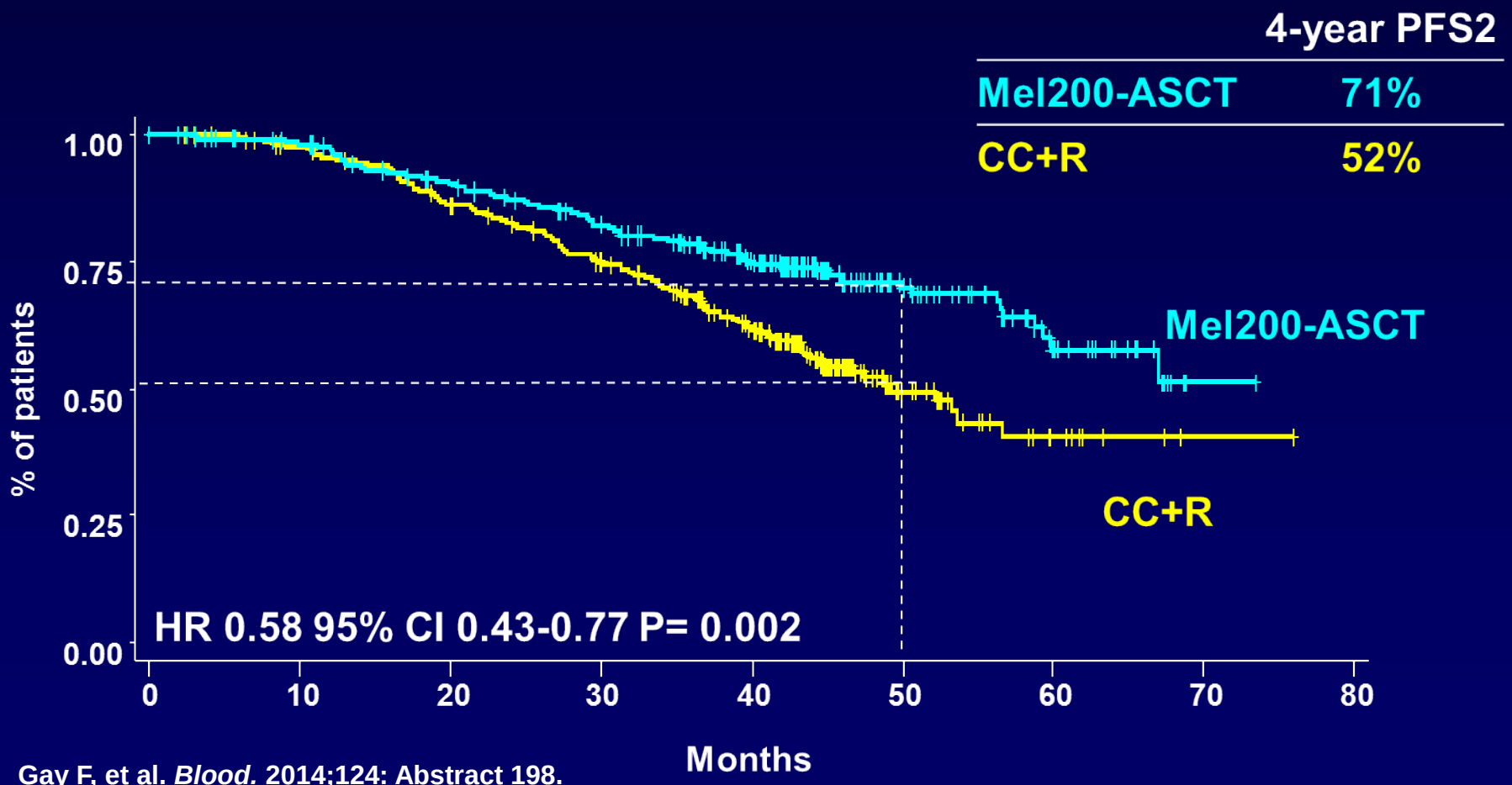
IMIDs, immunomodulatory agents

Mel200-ASCT vs CC+R: PFS2

Median follow-up from randomization: 4 years

PFS2: from random to second progression

First line	Second line	Subsequent lines	Death



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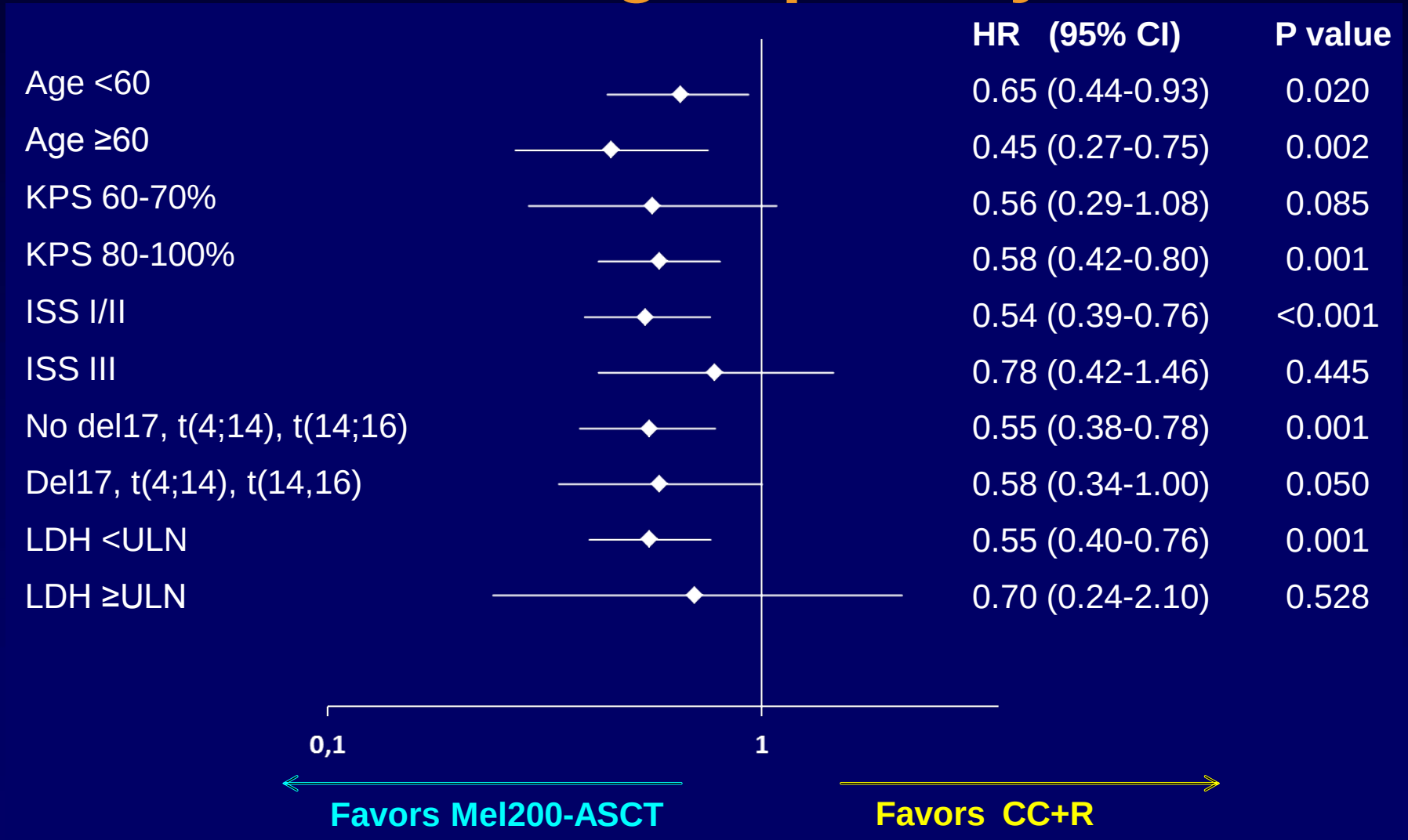
Mel200-ASCT vs CC+R: PFS2 Subgroup Analysis



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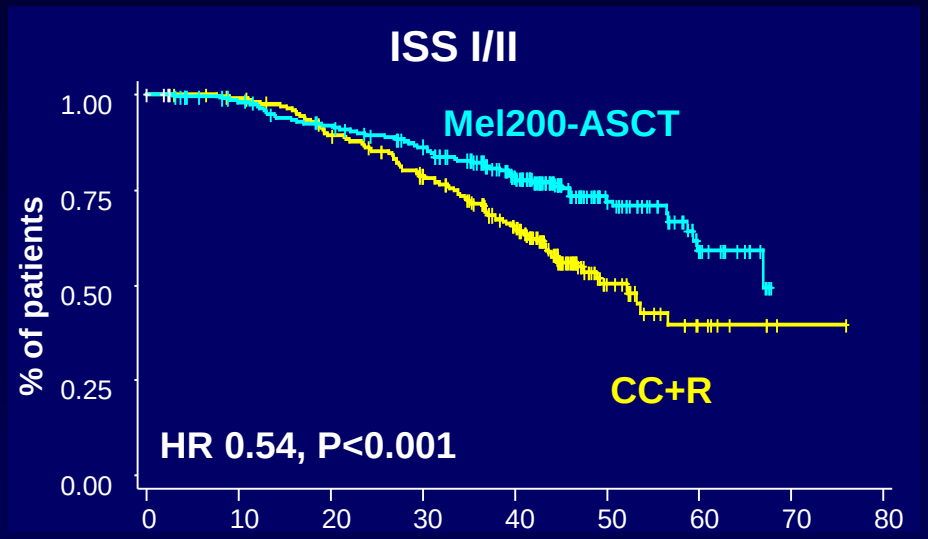
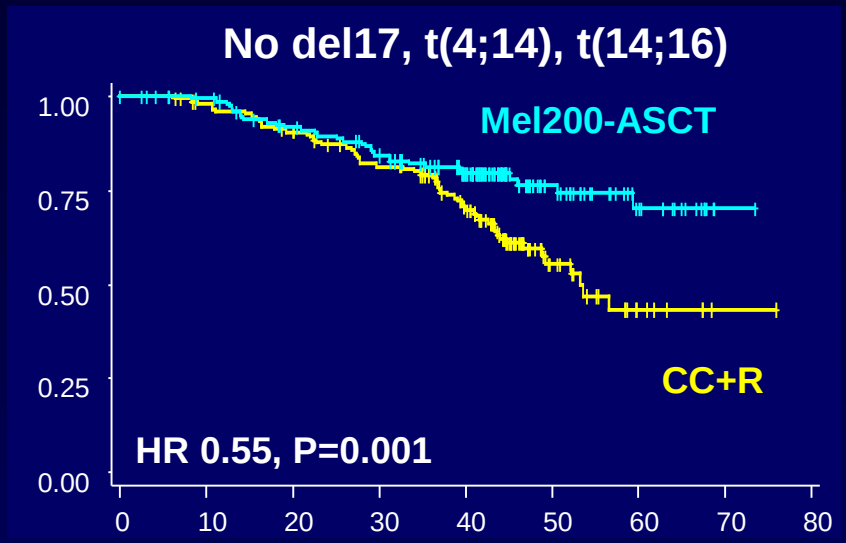
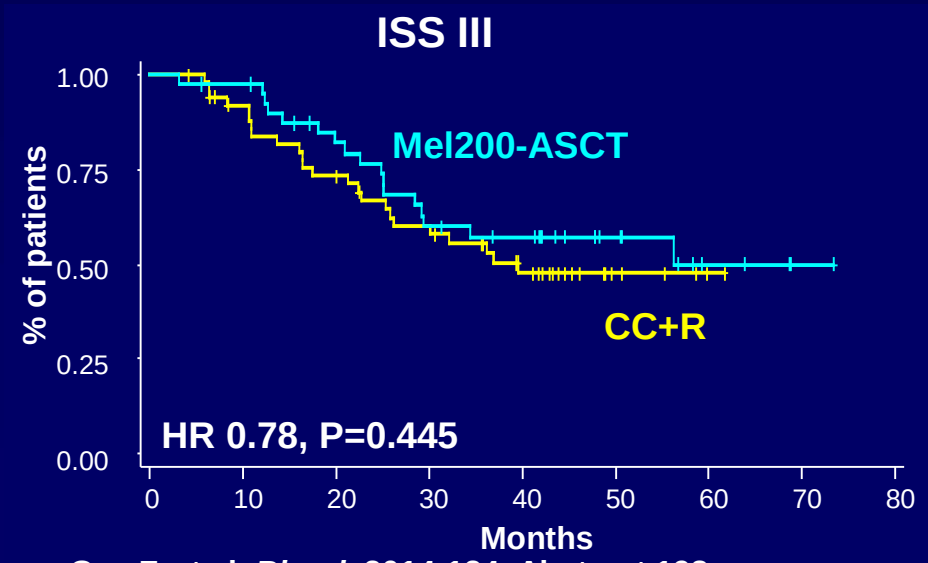
Mel200-ASCT vs CC+R: PFS2 Subgroup Analysis

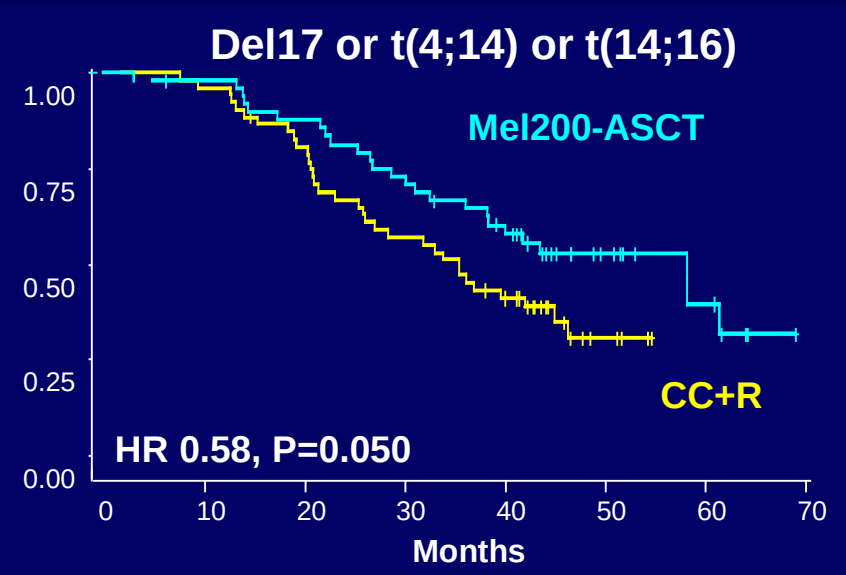
Good Prognosis





Bad Prognosis





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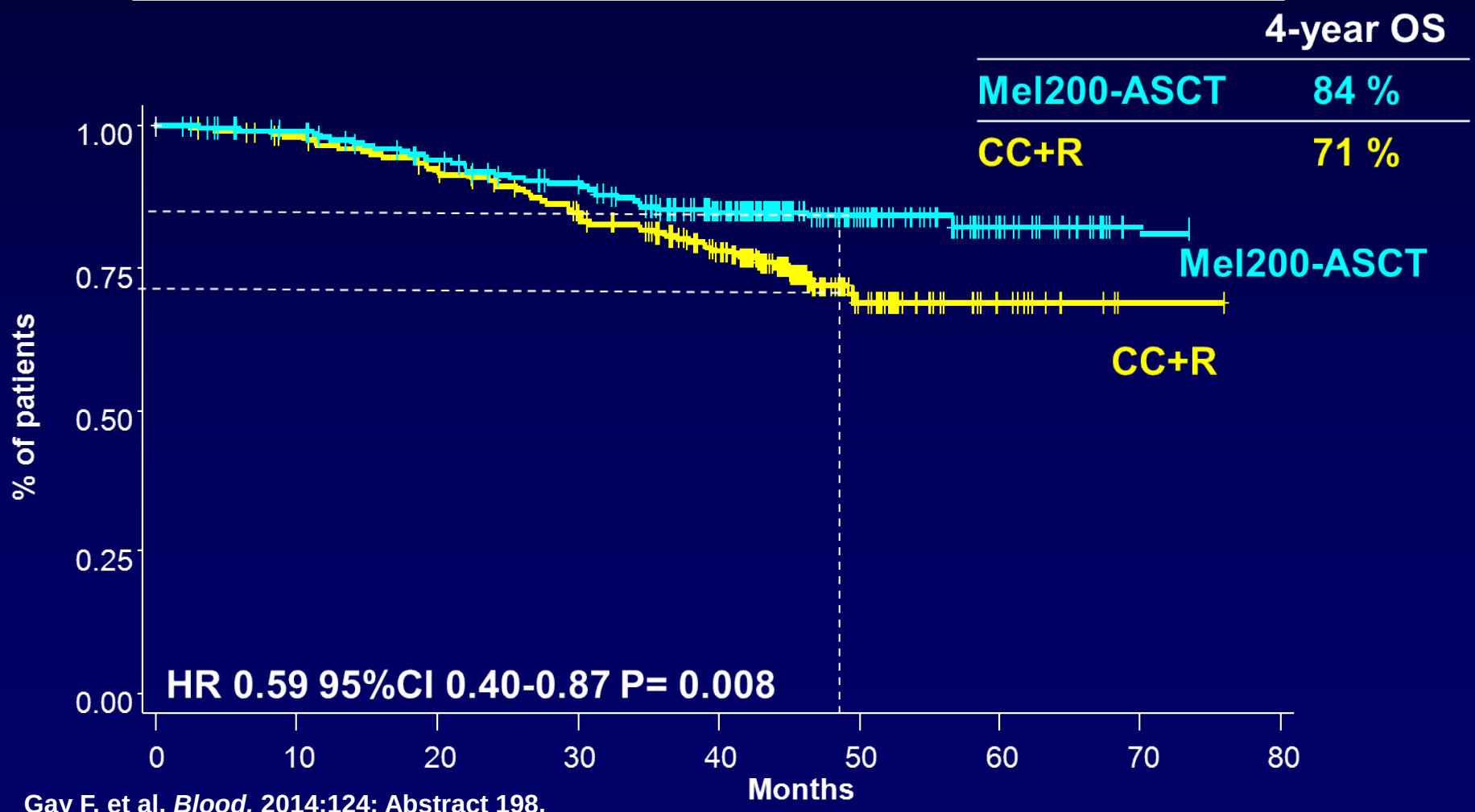
Mel200-ASCT vs CC+R: OS

Median follow-up from randomization: 4 years

OS: from random to death

First line	Second line	Subsequent lines	Death



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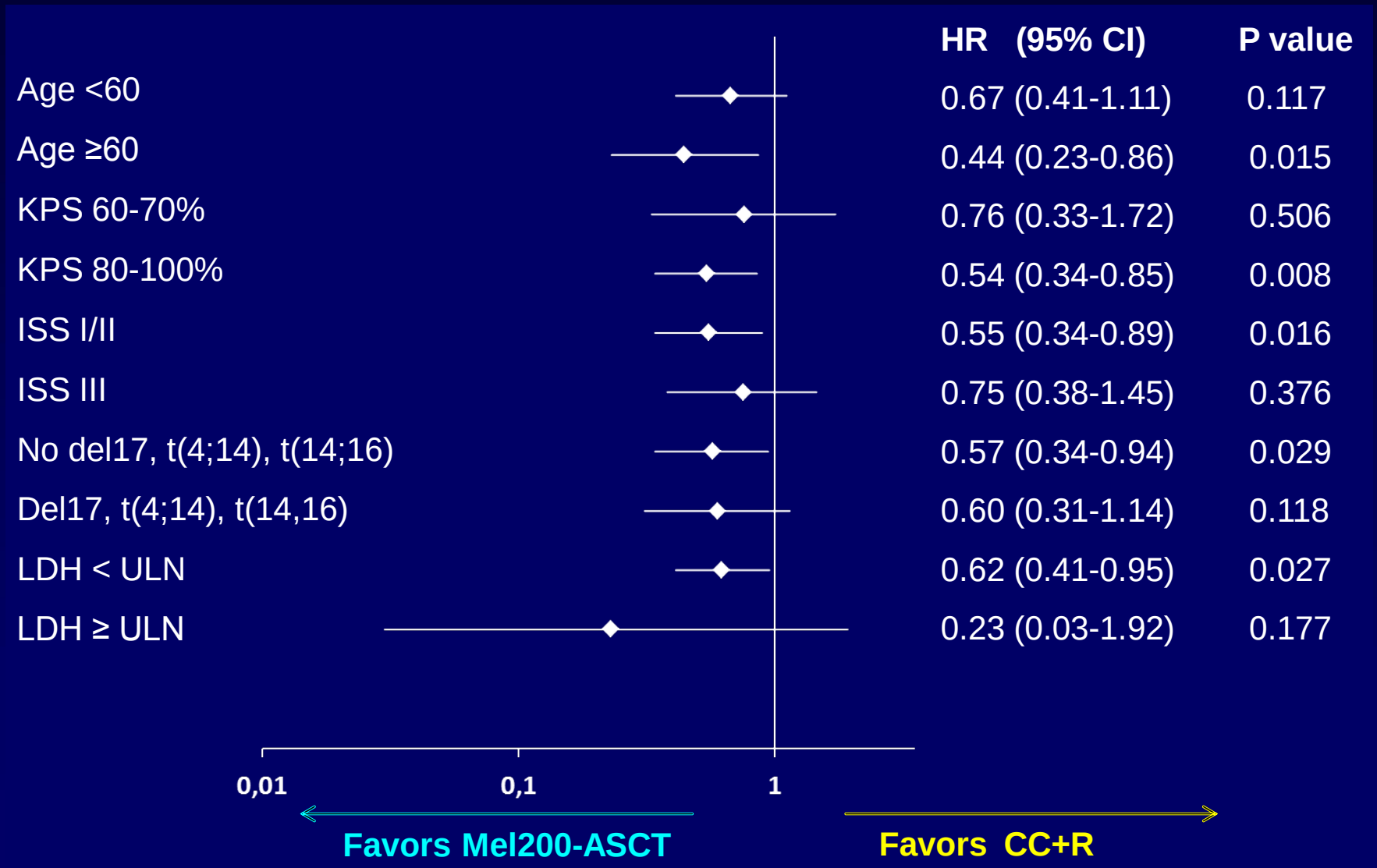
Mel200-ASCT vs CC+R: OS Subgroup Analysis



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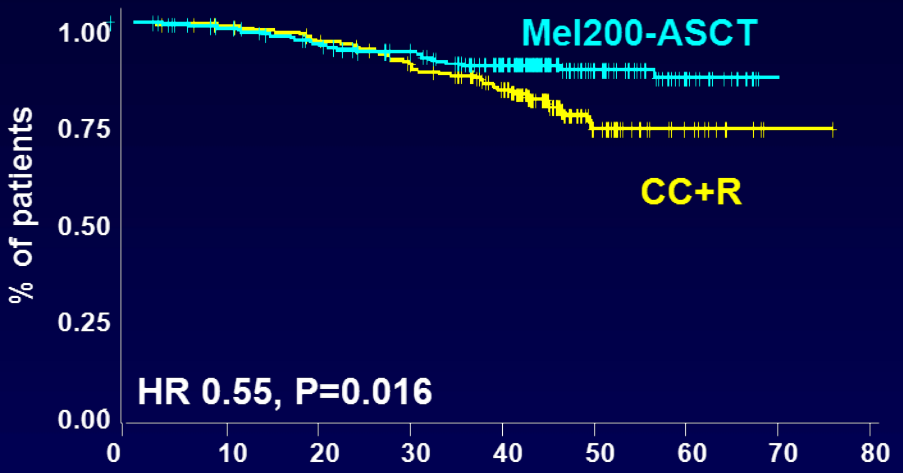
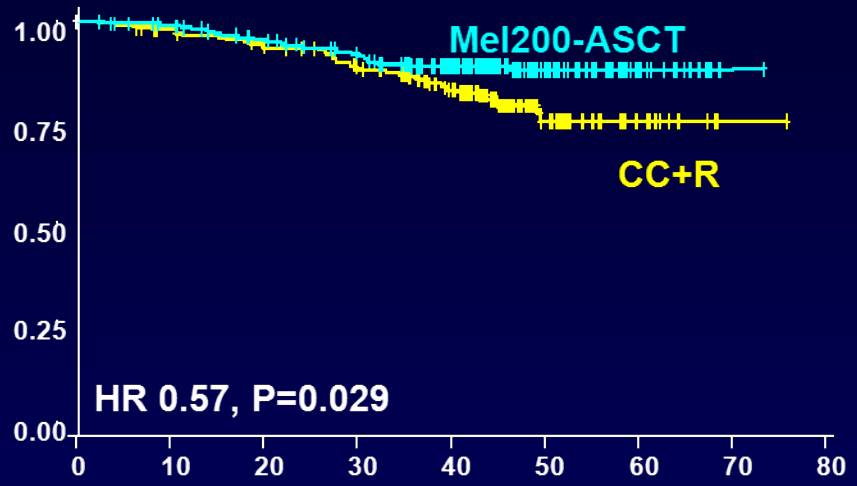
Mel200-ASCT vs CC+R: OS Subgroup Analysis

Good prognosis

ISS I/II

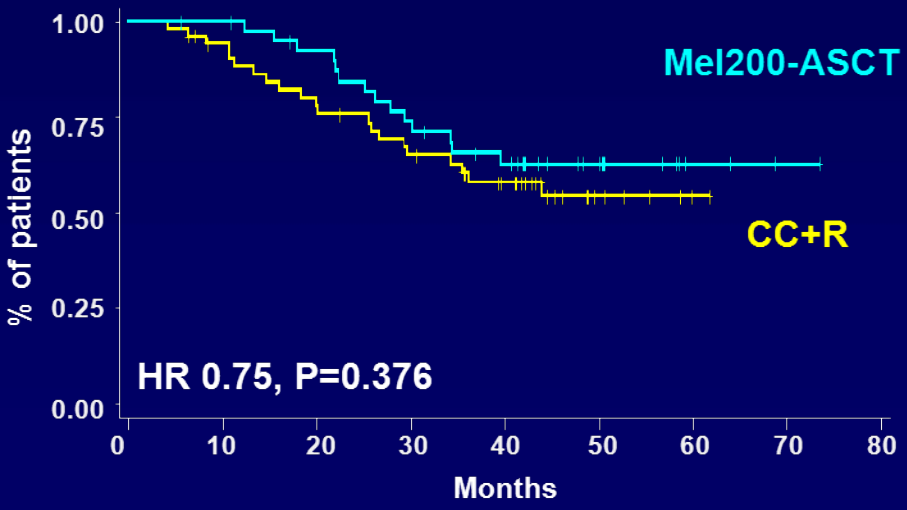


No del17, t(4;14), t(14;16)

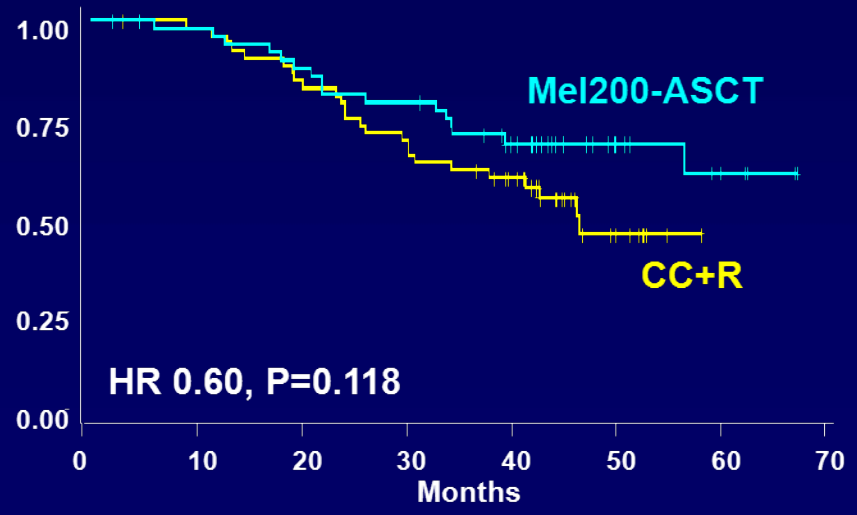


Bad prognosis

ISS III



Del17 or t(4;14) or t(14;16)



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Conclusions

- **Mel200-ASCT vs CC+R significantly prolongs PFS1, PFS2, andd OS in comparison with CC+R**
- **ASCT as salvage therapy may not be feasible in all patients**
- **The major benefit of Mel200-ASCT vs CC+R was shown in patients with good prognosis**

  → Intensified treatment to prolong OS
- **Bad prognosis patients require more effective treatment**

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