IMPROVED OVERALL SURVIVAL WITH AUTOLOGOUS TRANSPLANT VS CYCLOPHOSPHAMIDE-LENALIDOMIDE-DEXAMETHASONE IN NEWLY DIAGNOSED MYELOMA: A PHASE 3 TRIAL

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EMN Trialist Group

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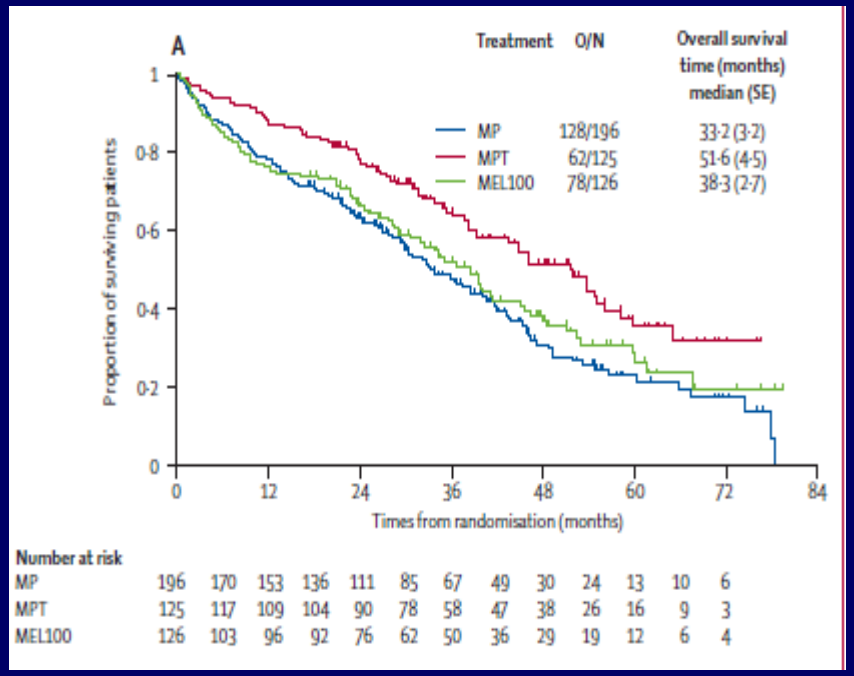
Presentation includes discussion of the off-label use of a drug or drugs

Rationale

ASCT vs Conventional chemotherapy + novel agents

MPT vs MEL100-ASCT[1]

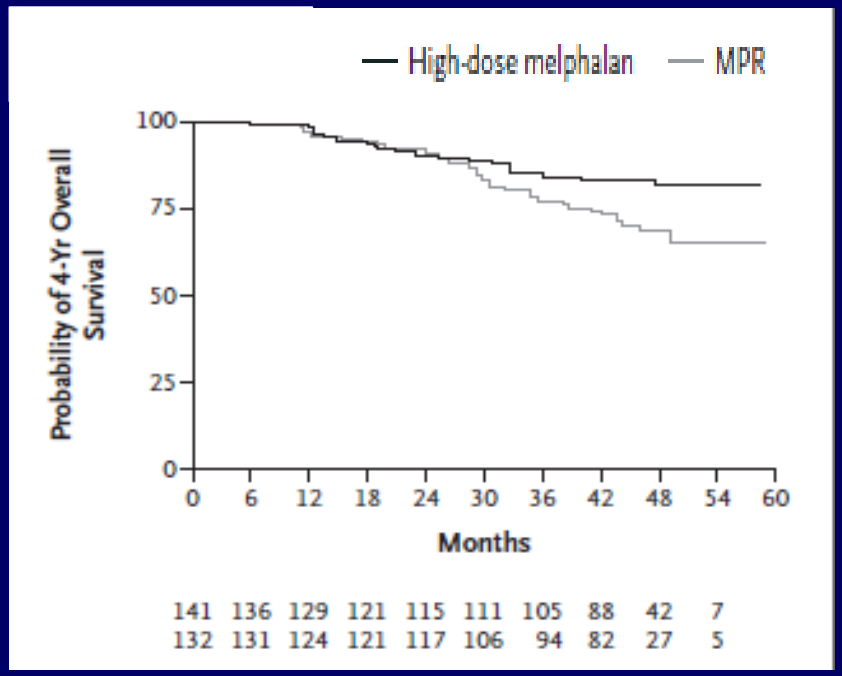
Age 65-75 years



MPT vs MEL100-ASCT: HR 0.59, P=0.0006

MPR vs MEL200-ASCT[2]

Age ≤ 65 years



MEL200-ASCT vs MPR: HR 0.55, P=0.02

MP, melphalan-prednisone; MPT, MP plus thalidomide; MEL100-ASCT, melphalan 100 mg/m2 followed by autologous stem-cell transplantation; MEL200-ASCT, melphalan 200 mg/m2 followed by autologous stem-cell transplantation; MPR, melphalan-prednisone-lenalidomide

1. Facon T et al, Lancet 2007; 370: 1209-18. 2. Palumbo A et al, N Engl J Med 2014 371(10):895-905

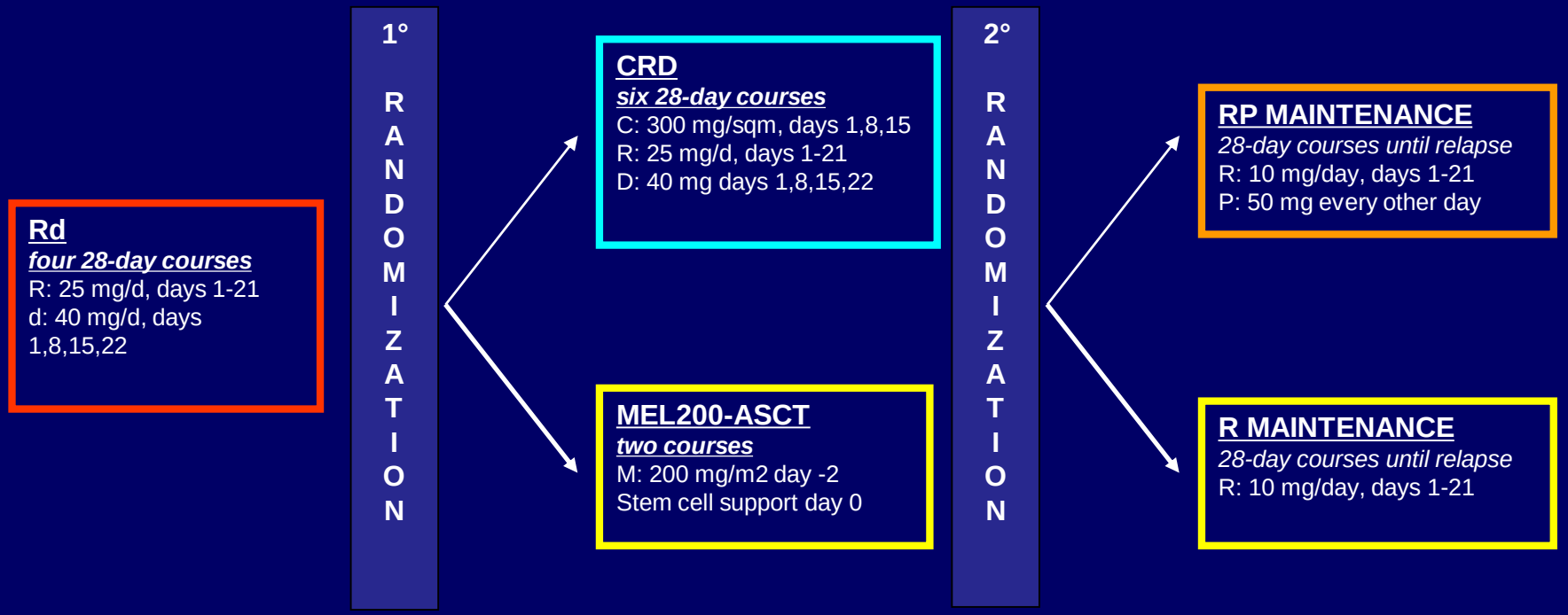
Aims

- **Efficacy MEL200-ASCT vs CRD**
  - **Progression-free survival**
  - **Overall survival**
- **Safety MEL200-ASCT vs CRD**
  - **Adverse Events**
  - **Second primary malignancies**

CRD: cyclophosphamide-lenalidomide-dexamethasone; MEL200-ASCT: melphalan 200 mg/m2 followed by autologous stem cell transplant

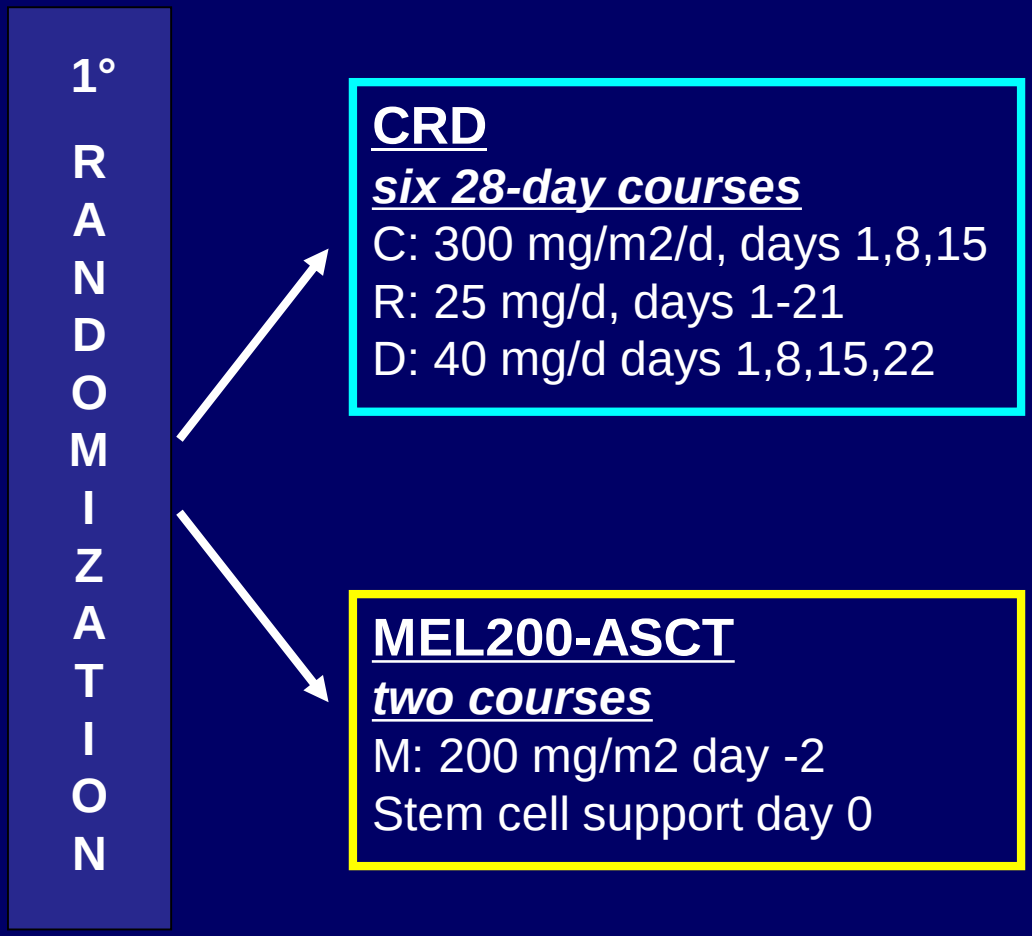
Treatment schedule

- 389 patients (younger than 65 years) randomized from 59 centers
- Patients: Symptomatic disease, organ damage (CRAB), measurable disease



R, lenalidomide; D, dexamethasone; C, cyclophosphamide; P, prednisone; Rd, lenalidomide-dexamethasone; CRD, cyclophosphamide-lenalidomide-dexamethasone; MEL200-ASCT, melphalan 200 mg/m^2 followed by autologous stem cell transplantation; RP lenalidomide-prednisone,

MEL200-ASCT vs CRD



CRD, cyclophosphamide-lenalidomide-dexamethasone; C, cyclophosphamide; D, dexamethasone; R, lenalidomide; MEL200-ASCT, melphalan 200 mg/m^2 followed by autologous stem-cell transplantation

Patient Characteristics

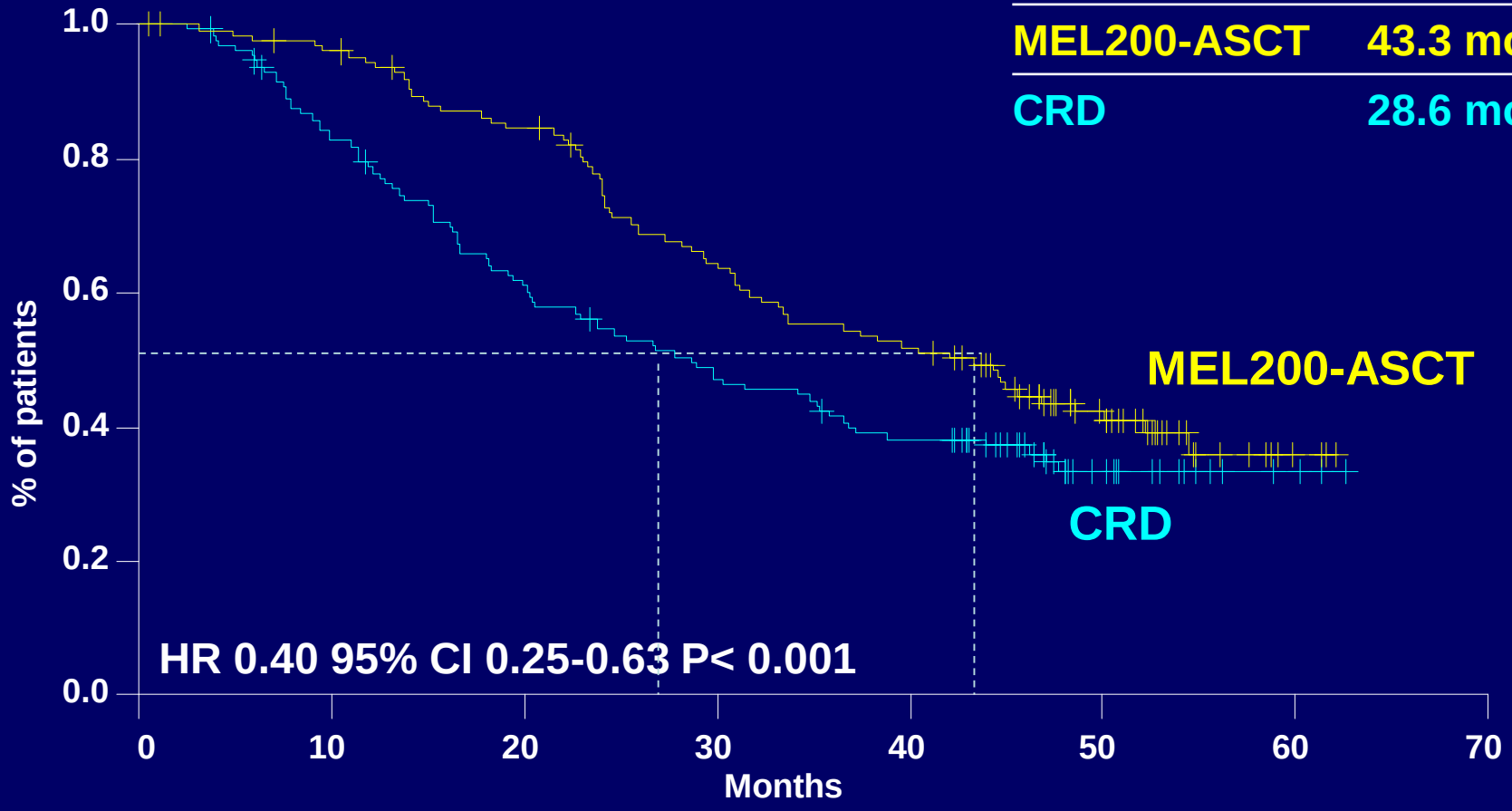
	MEL200-ASCT (n=127)	CRD (n=129)
Age		
median	57	56
>60 years	34	31
ISS Stage		
I	50%	45%
II	36%	37%
III	14%	18%
Chromosomal Abnormalities		
t (4;14)	9%	13%
t (14;16)	5%	5%
del 17	5%	8%
High-risk [t (4;14) or t(14;16) or del17]	18%	23%

CRD, cyclophosphamide-lenalidomide-dexamethasone; MEL200-ASCT, melphalan 200 mg/m^2 followed by autologous stem-cell transplantation; ISS, International Staging System

MEL200-ASCT vs CRD
Progression-free survival

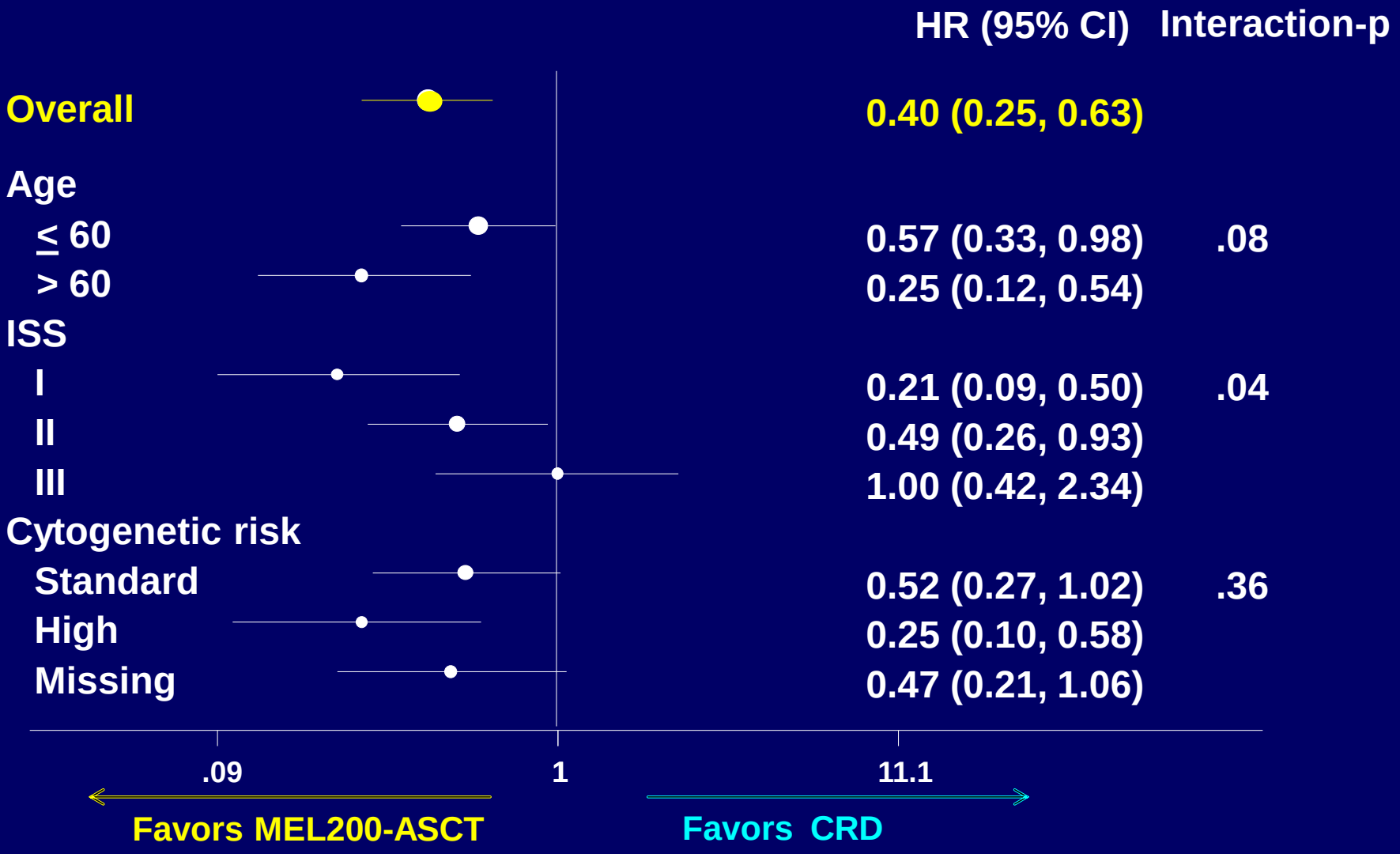
Median follow-up : 55 months

	Median PFS
MEL200-ASCT	43.3 months
CRD	28.6 months



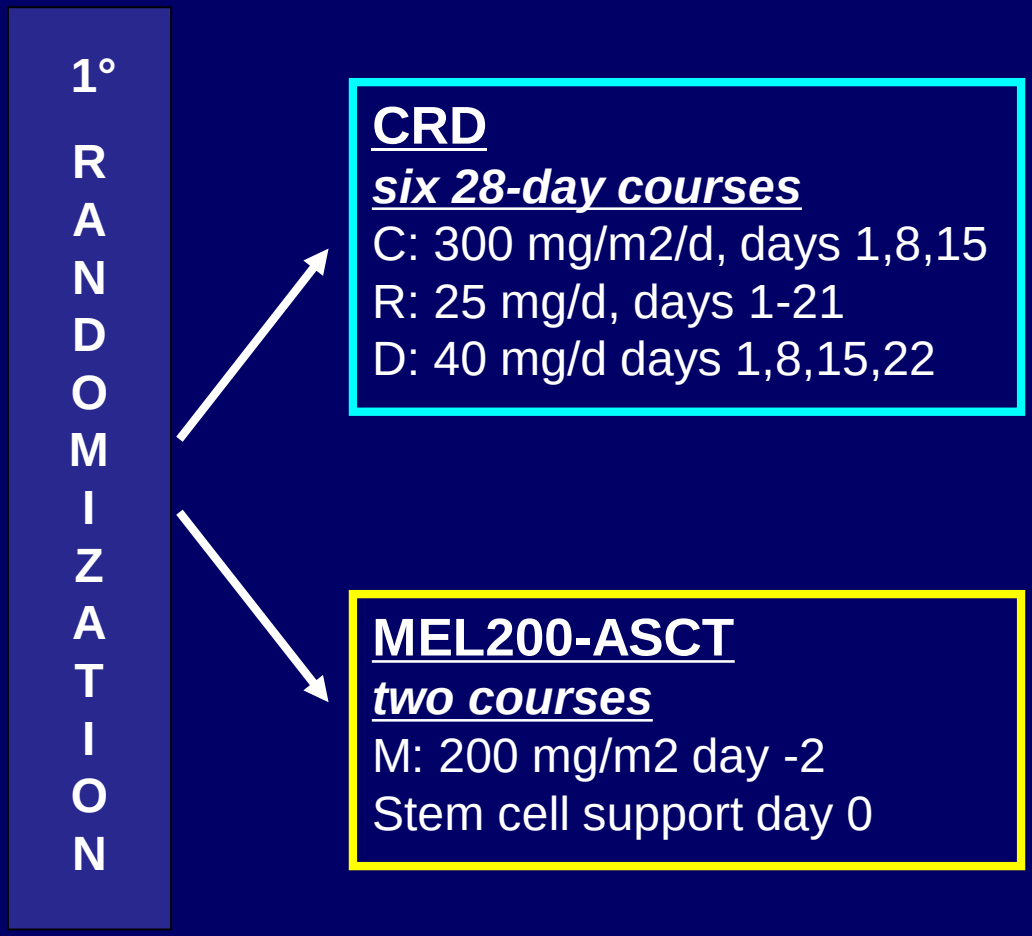
MEL200–ASCT, melphalan 200 mg/m2 followed by autologous stem cell transplantation; CRD cyclophosphamide lenalidomide dexamethasone; PFS, progression-free survival.

MEL200-ASCT vs CRD
Subgroup analyses of PFS



MEL200–ASCT, melphalan 200 mg/m2 followed by autologous stem cell transplantation; CRD cyclophosphamide lenalidomide dexamethasone; PFS, progression-free survival, ISS: International Staging System

MEL200-ASCT vs CRD



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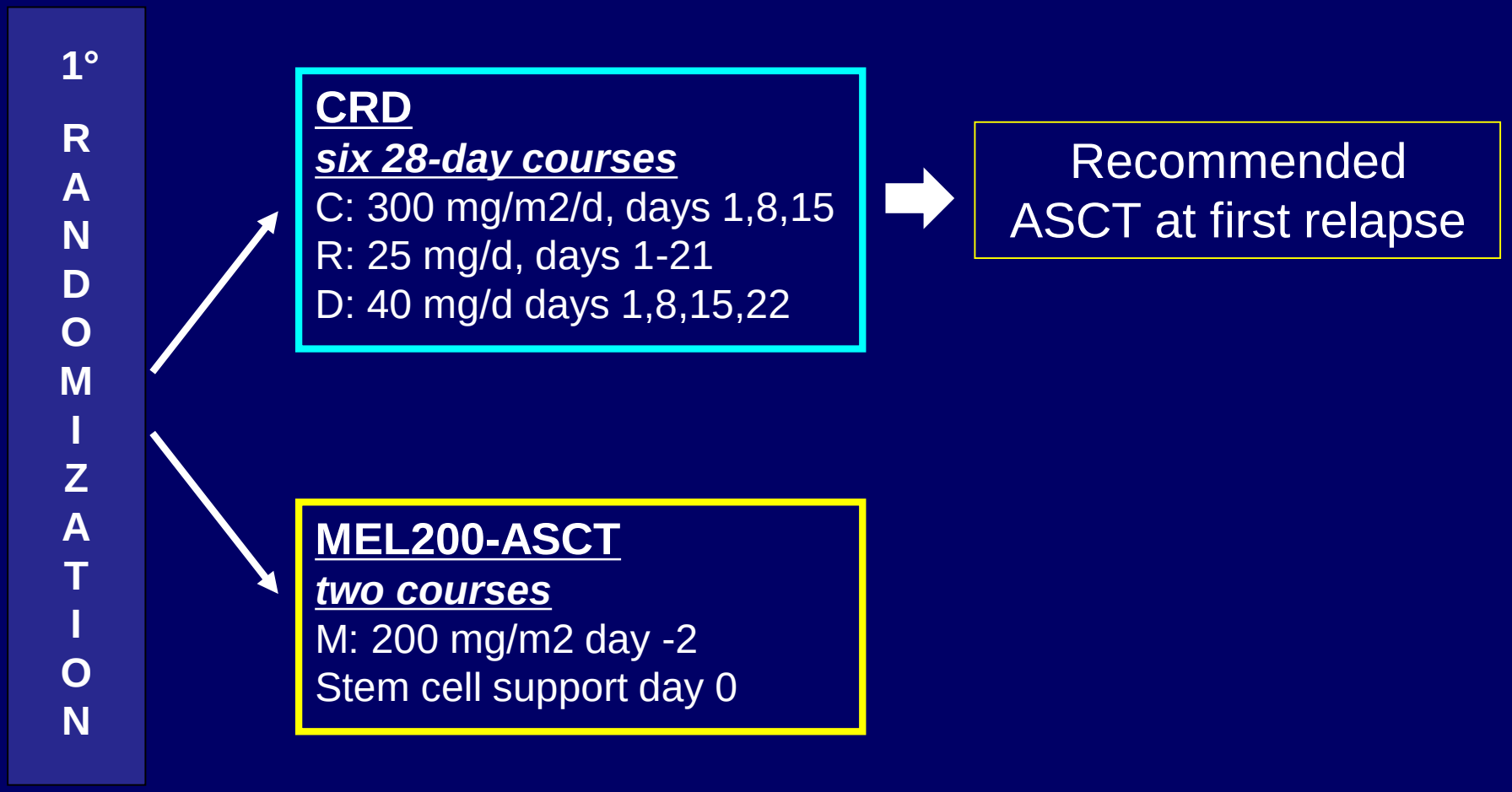
MEL200-ASCT vs CRD



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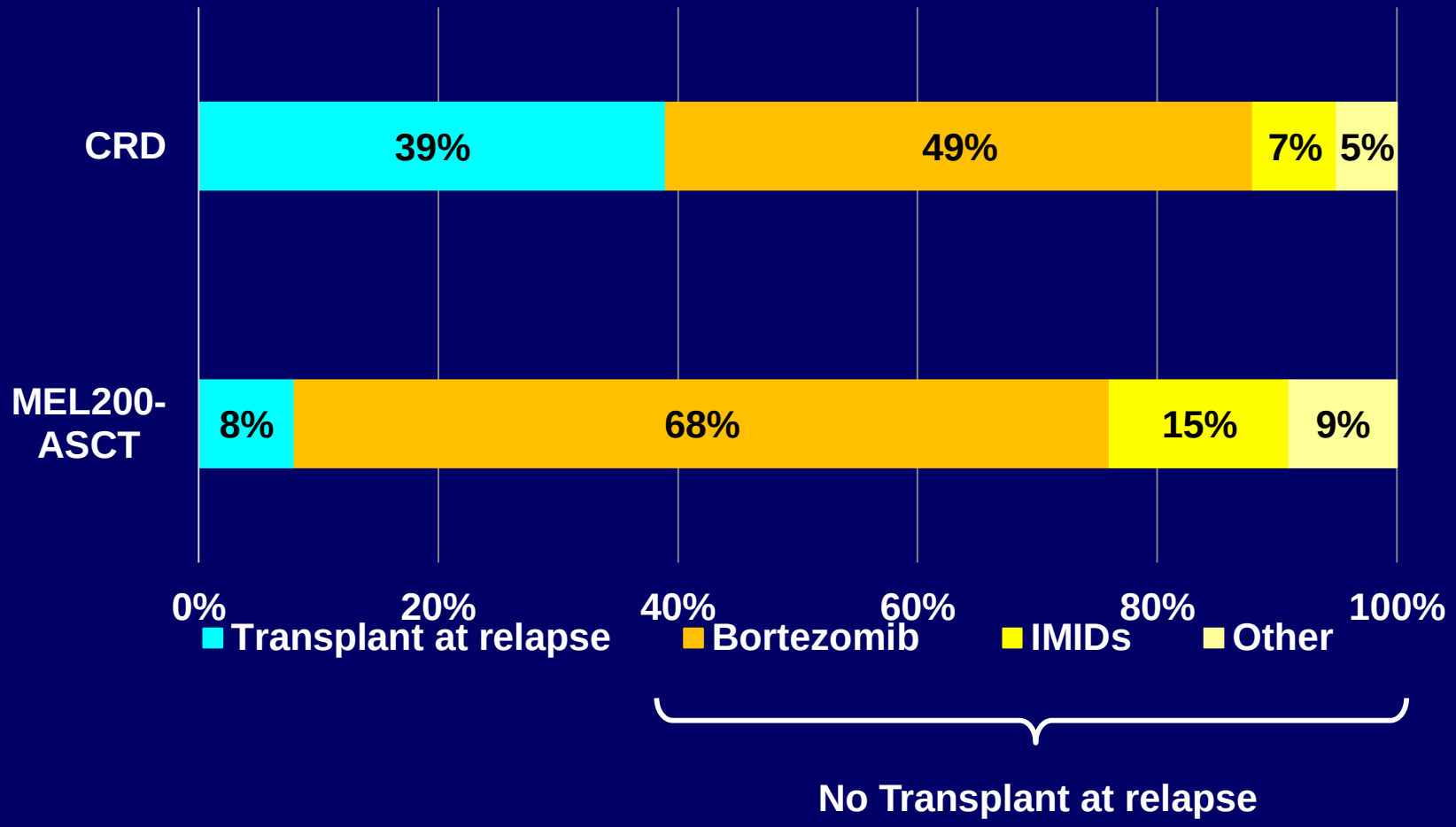
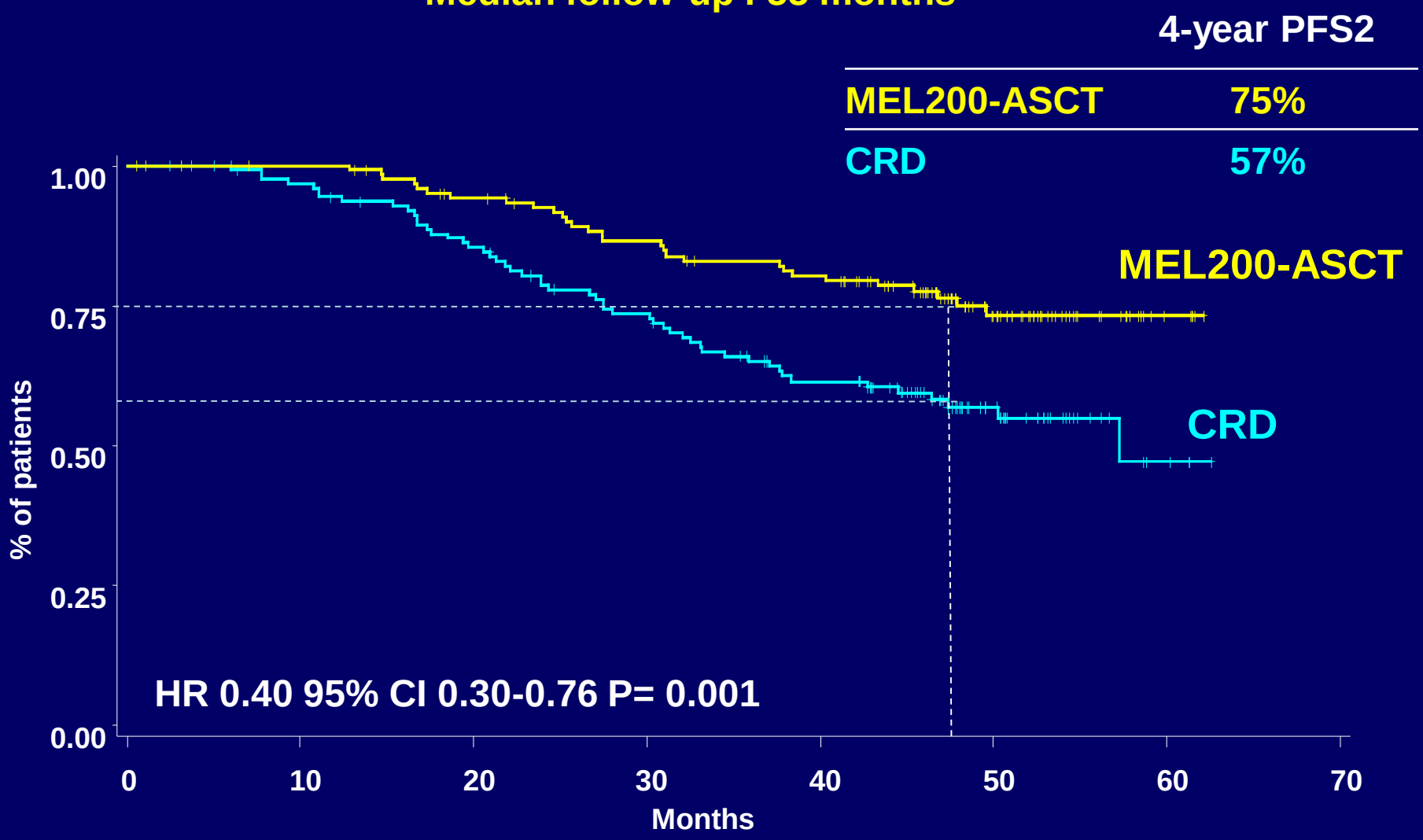
MEL200-ASCT vs CRD
Second-line therapy



MEL200 –ASCT, melphalan 200 mg/m2 followed by autologous stem cell transplantation; CRD, chyclophosphamide lenalidomide dexamethasone; IMIDs, immunomodulatory agents

Mel200-ASCT vs CRD
Progression-free survival-2

Median follow-up : 55 months

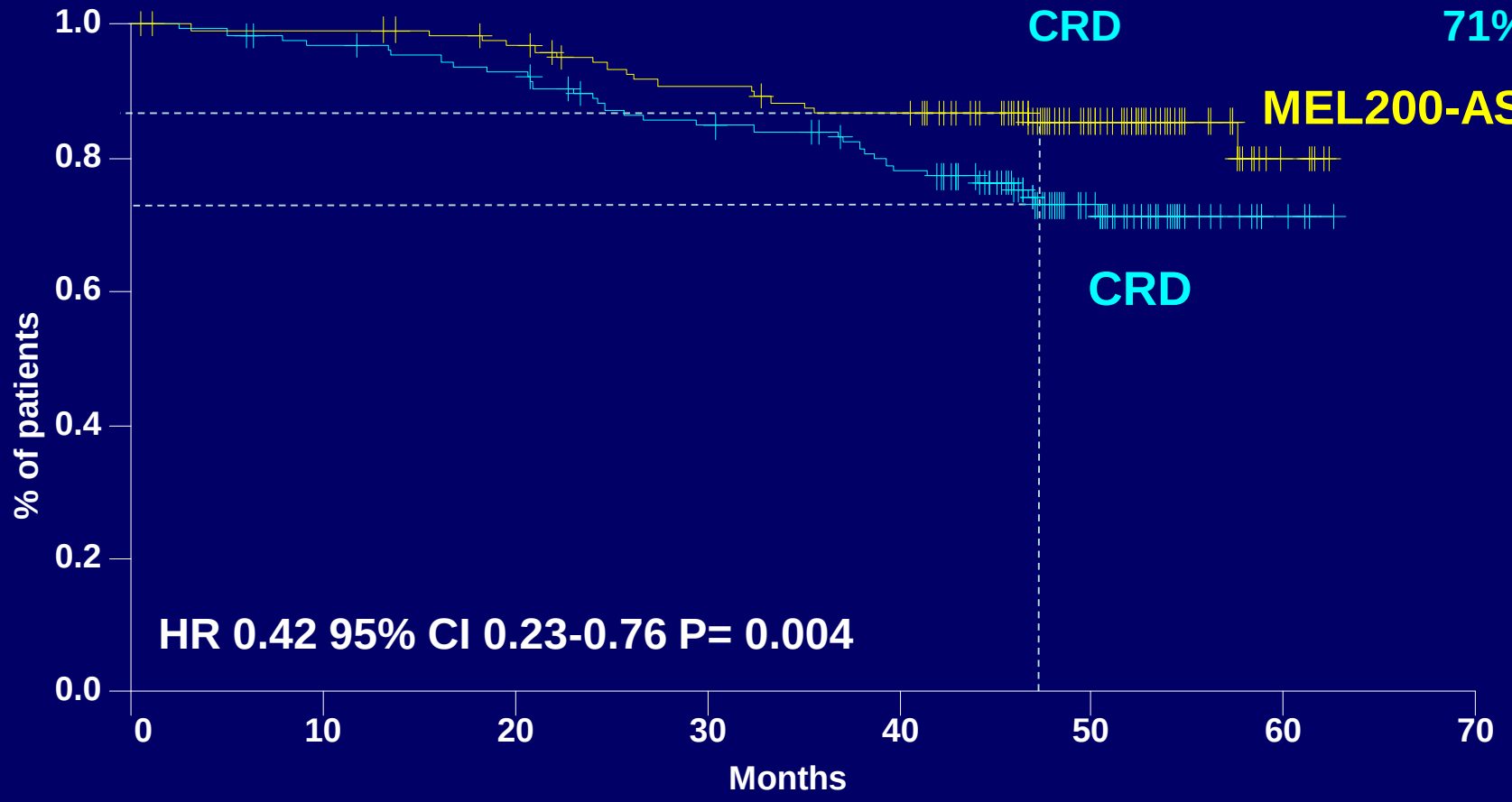


MEL200–ASCT, melphalan 200 mg/m2 followed by autologous stem cell transplantation; CRD cyclophosphamide lenalidomide dexamethasone; PFS, progression-free survival.

MEL200-ASCT vs CRD
Overall survival

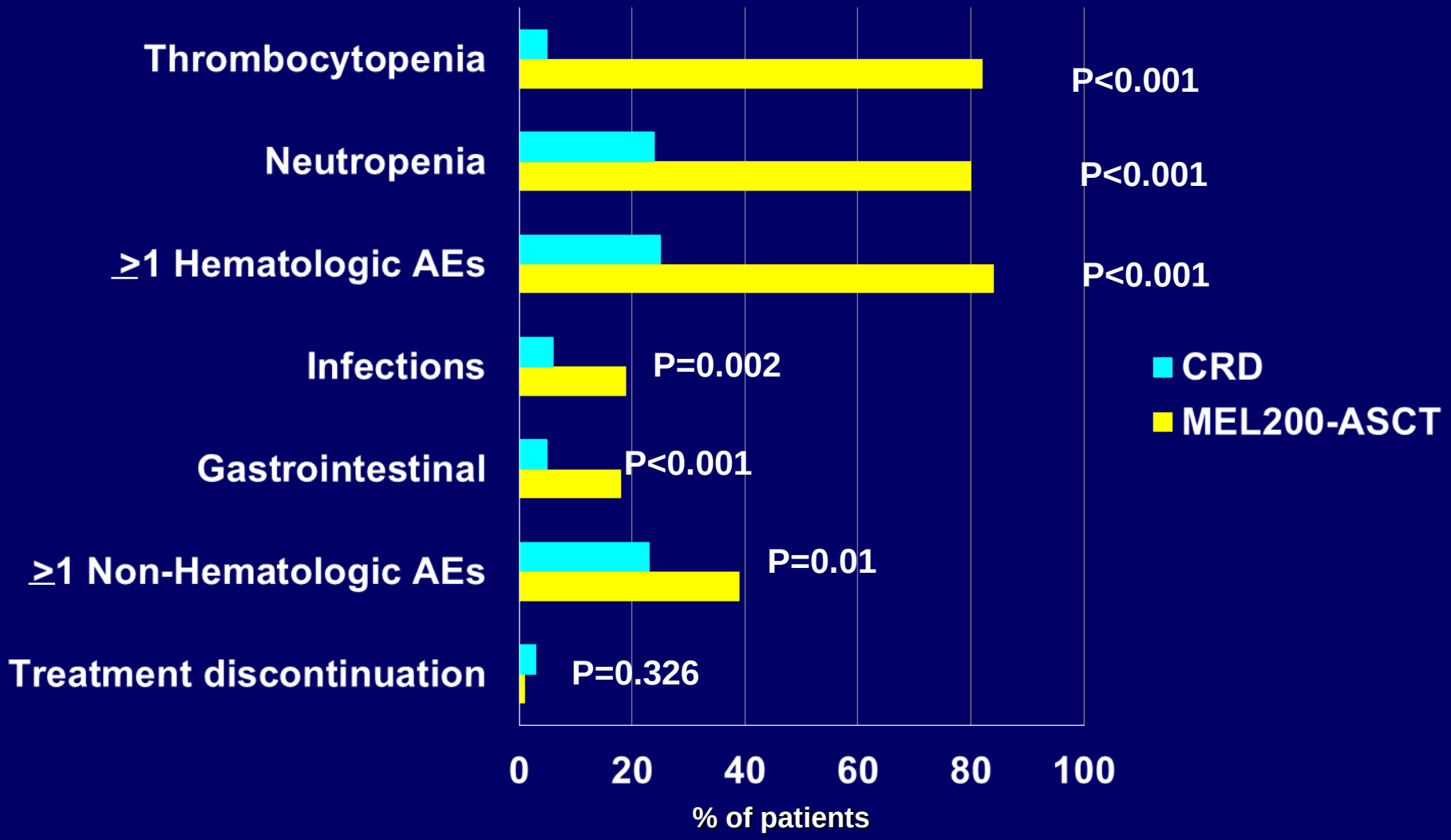
Median follow-up : 55 months

	4-year OS
MEL200-ASCT	86%
CRD	71%



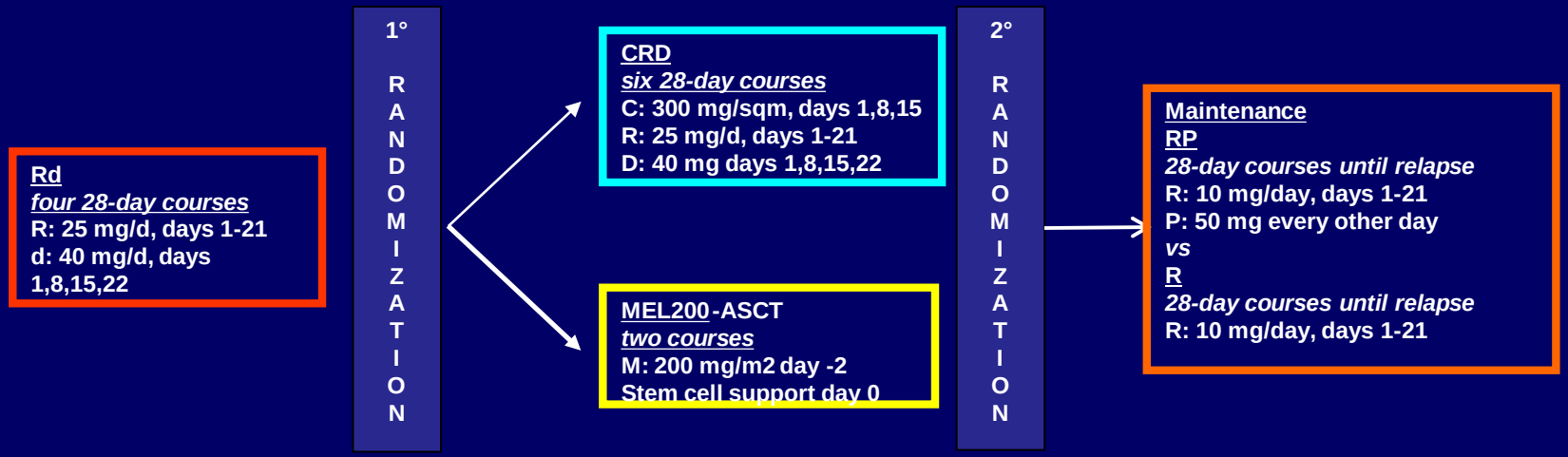
MEL200–ASCT, melphalan 200 mg/m2 followed by autologous stem cell transplantation; CRD cyclophosphamide lenalidomide dexamethasone; OS, overall survival.

MEL200-ASCT vs CRD
Grade 3-4 AEs



CRD, cyclophosphamide-lenalidomide-dexamethasone; MEL200-ASCT, melphalan 200 mg/m^2 followed by autologous stemm cell transplantation; AEs adverse events

Discontinuation for AEs and SPM



	Induction	Consolidation		Maintenance	
	Rd	MEL200-ASCT	CRD	MEL200-ASCT	CRD
Discontinuation for AEs	5%	1%	4%	7%	6%
N° of SPM					
- Hematologic	0	0	0	0	0
- Solid	3	0	0	3	4
- Skin cancer	1	0	0	6	1

R, lenalidomide; D, dexamethasone; C, cyclophosphamide; P, prednisone; Rd, lenalidomide-dexamethasone; CRD, cyclophosphamide-lenalidomide-dexamethasone; MEL200-ASCT, melphalan 200 mg/m^2 followed by autologous stem cell transplantation; RP lenalidomide-prednisone; AEs adverse events; SPM, second primary malignancies

Conclusions

Efficacy

	MEL200-ASCT	CRD	P value
✓ **Median PFS**	43.3 months	28.6 months	<0.001
✓ **4-year PFS2**	75%	57%	0.001
✓ **4-year OS**	86%	71%	0.004

Safety	MEL200-ASCT	CRD	P value
✓ **Grade 3-4 Hematologic AEs**	84.3%	26.4%	<0.001
✓ **Grade 3-4 non-hematologic AEs**	38.6%	23.3%	0.01
✓ **Treatment discontinuation**	1%	4%	0.326

MEL200–ASCT, melphalan 200 mg/m2 followed by autologous stem cell transplantation; CRD cyclophosphamide lenalidomide dexamethasone; PFS, progression-free survival, OS, overall survival; AE: adverse event.

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