

Allogeneic stem cell transplantation for High-Risk Myeloma



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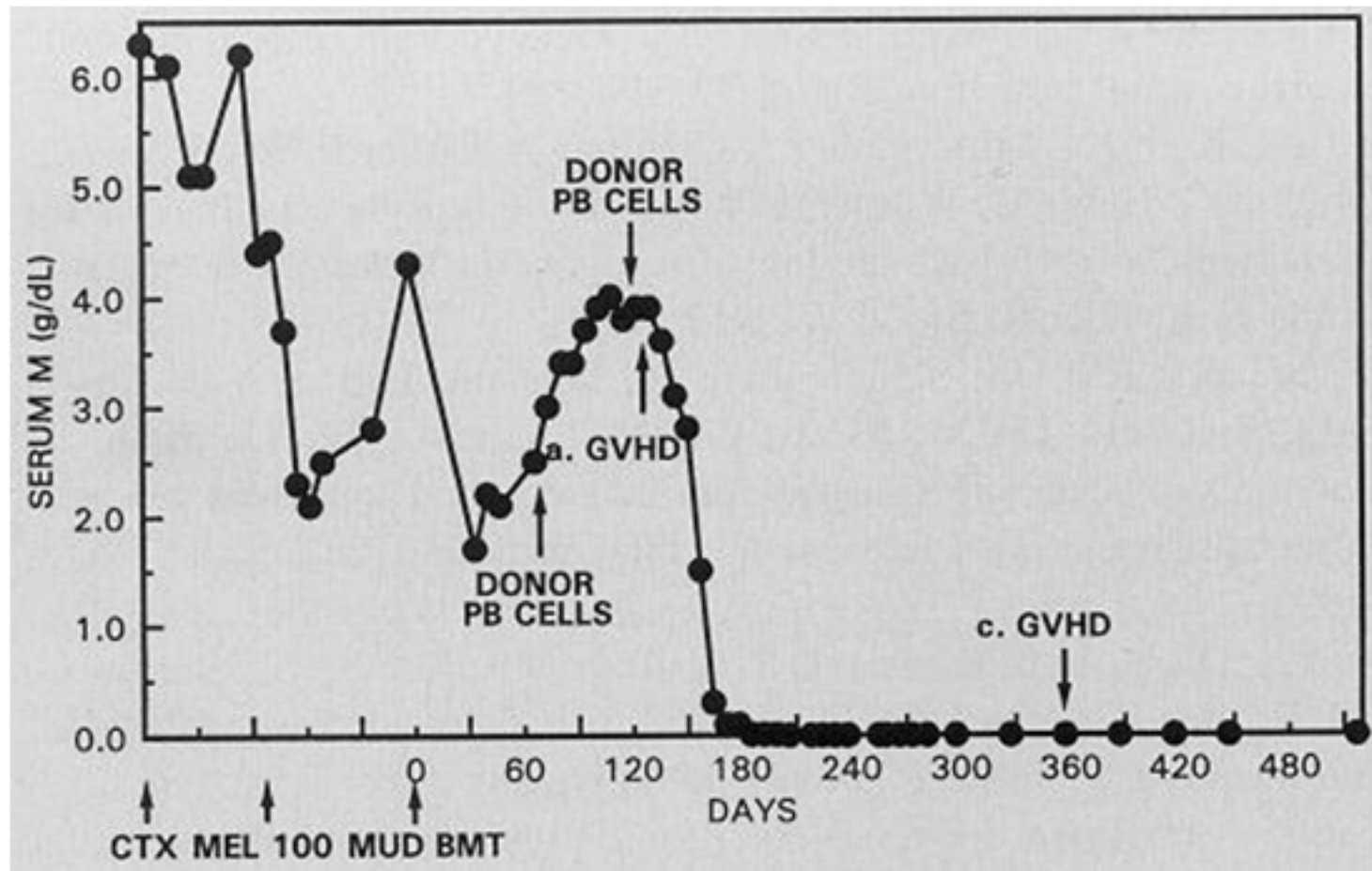
Allo-SCT for MM

- Is there a GvM Effect ?
- Curative Treatment Option ?
- Allogeneic SCT as front-line therapy (comparison to autologous SCT)?
 - for high risk disease
- Strategies to improve Allo-SCT
 - Reduce TRM
 - Increase GvM

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Graft-versus Myeloma Effect



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Allogeneic Stem cell transplantation for MM

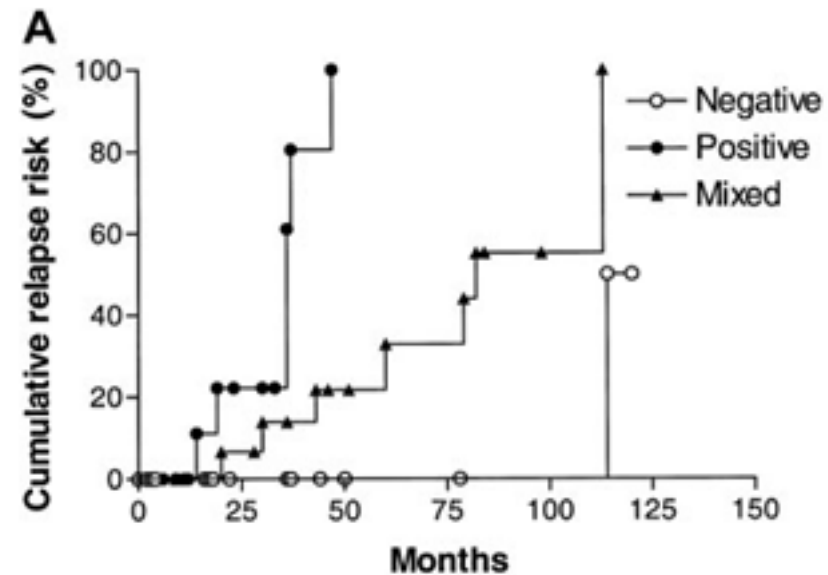
Response Quality correlates with OS

Progression depending on Response Quality

Response Quality

Status

	PCR-	PCR+
<u>CCR</u>	94%	54%
<u>Progress</u>	6%	46%

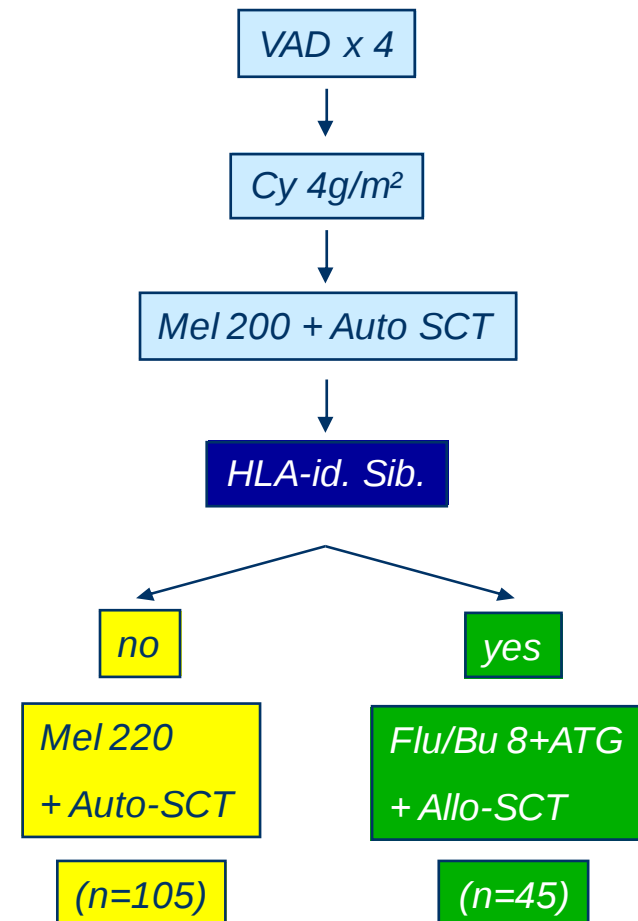


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Tandem-Melphalan vs. Auto/Mini-Allo SCT for High Risk Myeloma IFM 99-03/04

1. Only High Risk Patients
(13q deletion + $\beta_2m > 3\text{mg/l}$)
2. Suboptimal Conditioning
(High dose ATG-GvM?)

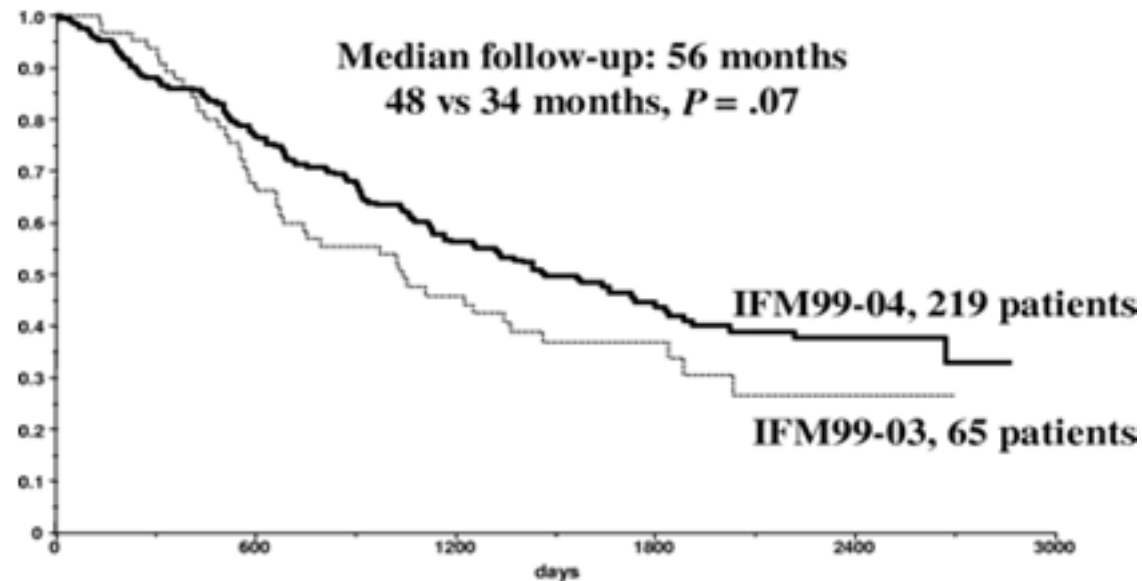


Tandem-Melphalan vs. Auto/Mini-Allo SCT for High Risk Myeloma

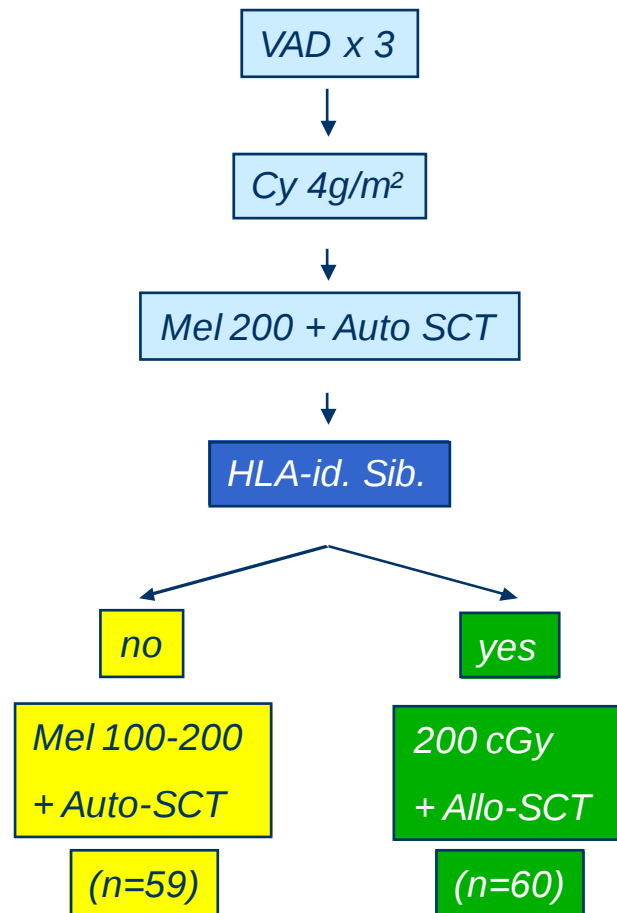
Results

	Tandem-Mel (n=85)	Auto-allo-SCT (n=81)	p
CR-Rate after 2nd SCT	31%	35%	0.62
TRM	5%	10.9%	0.51
Median OS at 41 Mo	46%	51%	0.90

Overall Survival



Allogeneic SCT for young patients with newly diagnosed MM (all patients – no risk group)

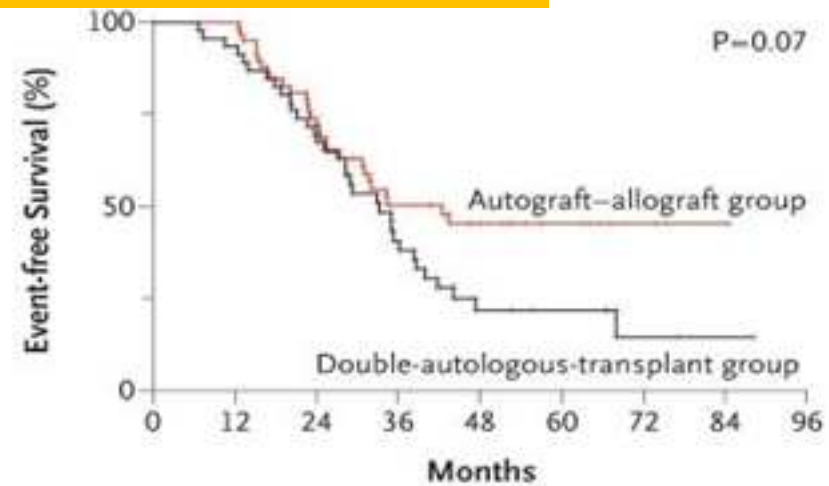
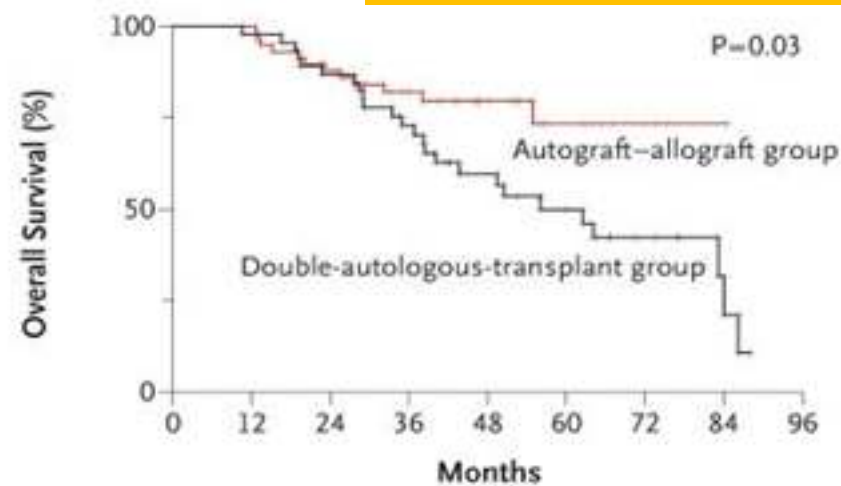


1. *Conditioning in Auto-Arm Suboptimal (Mel 100 in 20 patients, additional patients received 140 instead of 200 mg/m²)*

Tandem-HD-Melphalan vs. Auto-Allo-SCT for Patients with newly diagnosed MM Results

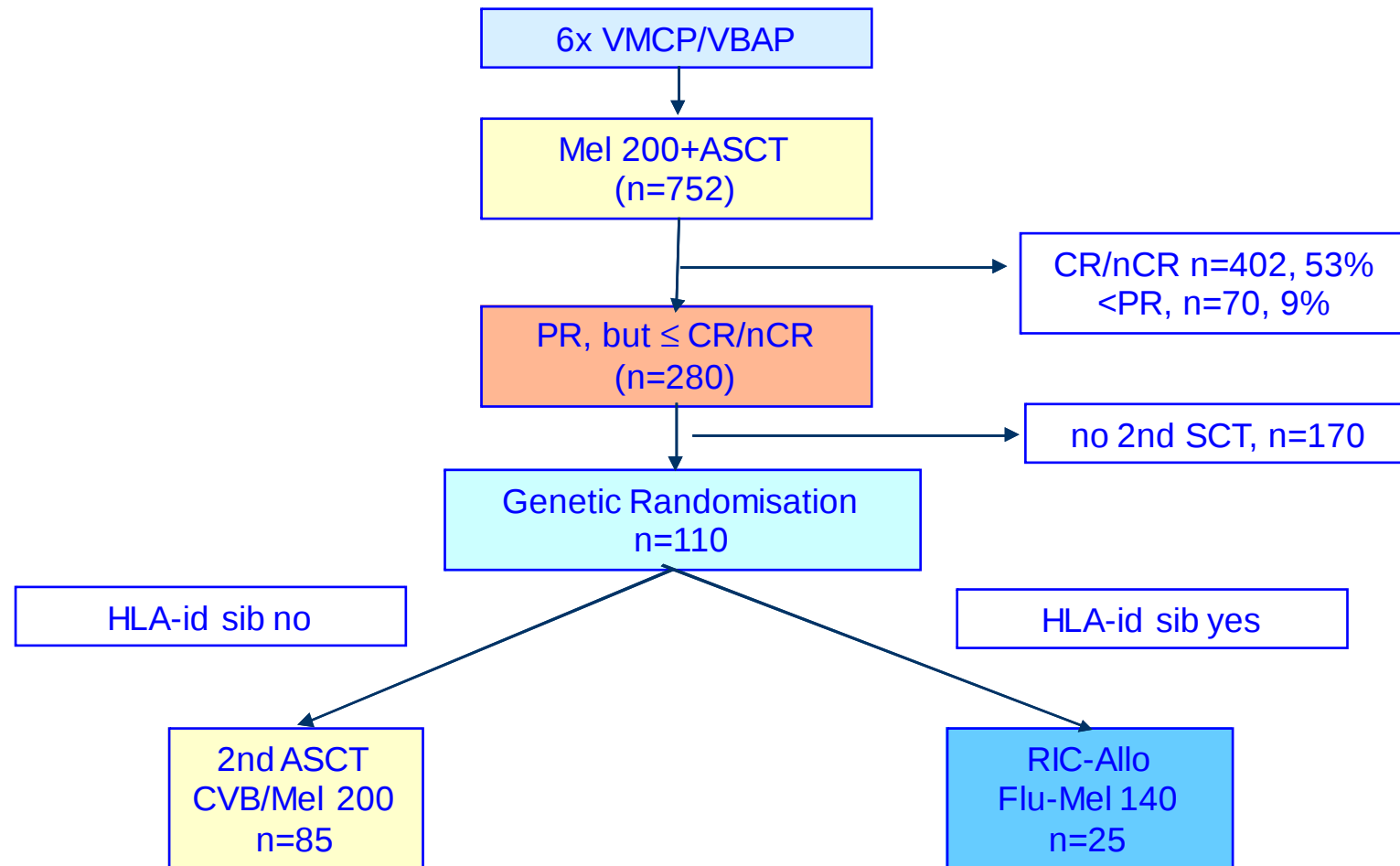
	Tandem-Mel (n=46)	Auto-allo-SCT (n=58)	p
CR-Rate after 2nd SCT	26%	55%	0.004
TRM after 2 years	2%	10%	> 0.05
Acute GvHD-Rate (I - IV)	n.a.	43%	n.a.
Relapse mortality	43%	7%	<0.001
Median OS at 46 Mo	58 Mo	not reached	0.03

→ In this study neither 13q del nor β_2m impacted on outcome of Allo-SCT



PETHEMA study

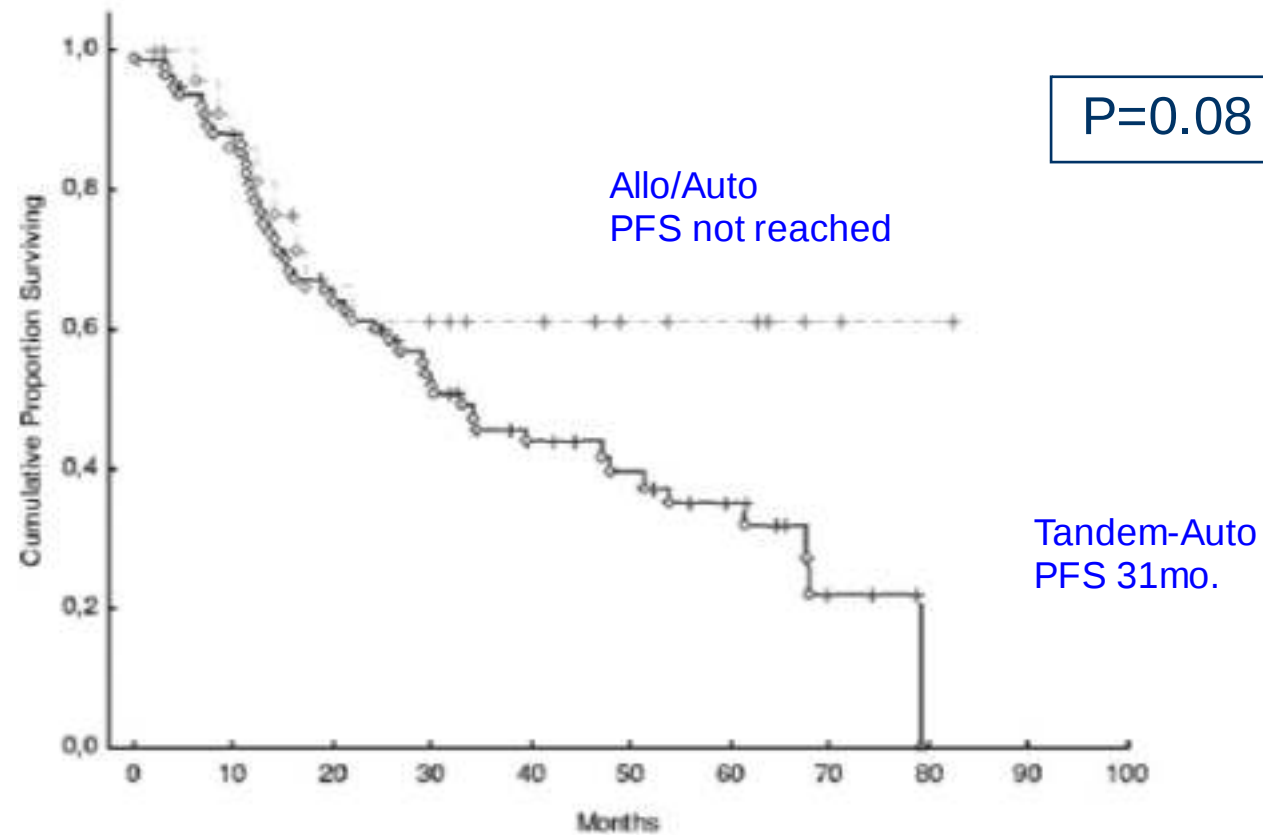
Newly diagnosed MM, age ≤ 65 yrs.



PETHEMA study

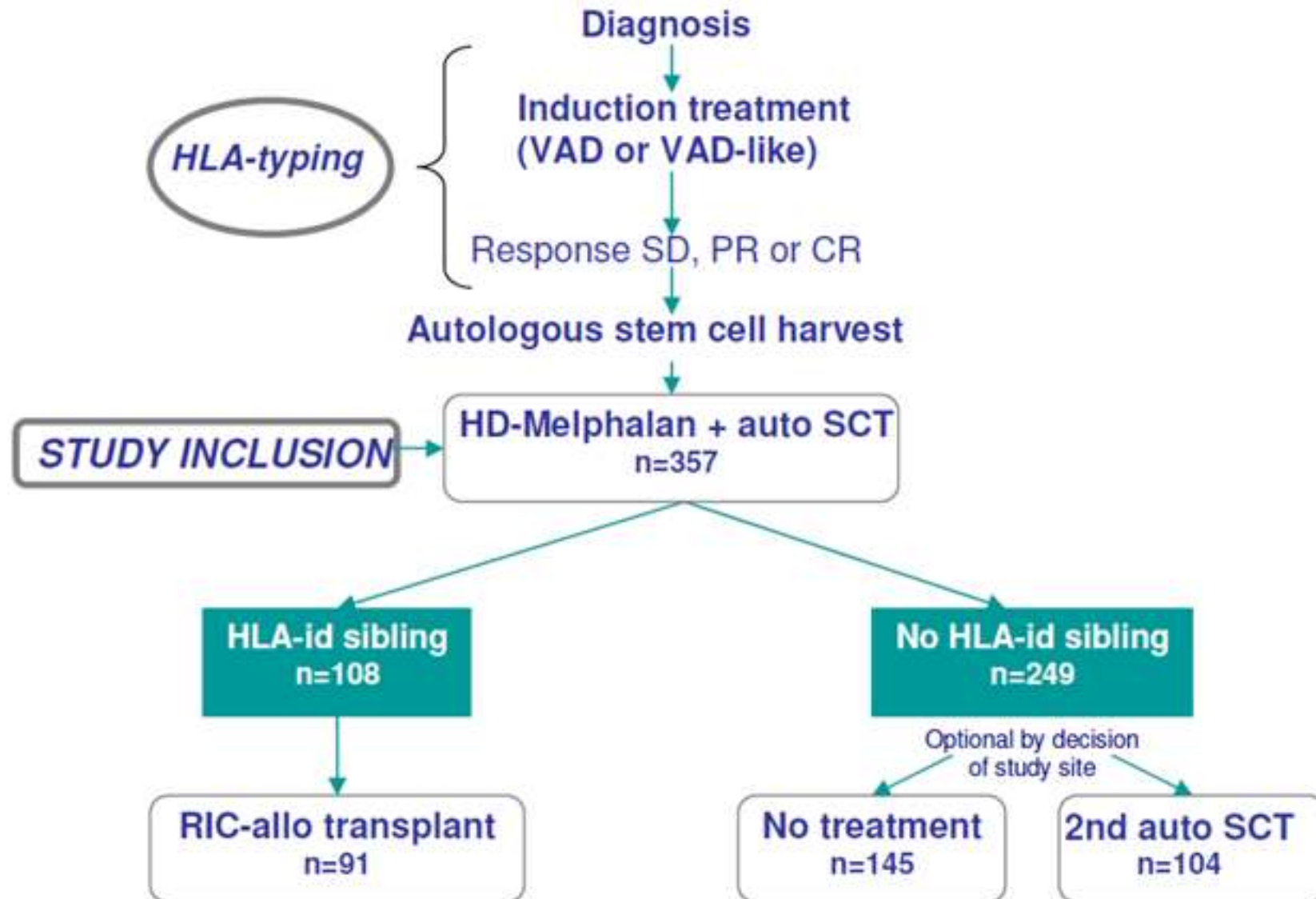
Newly diagnosed MM, age ≤ 65 yrs.#

Progression Free Survival



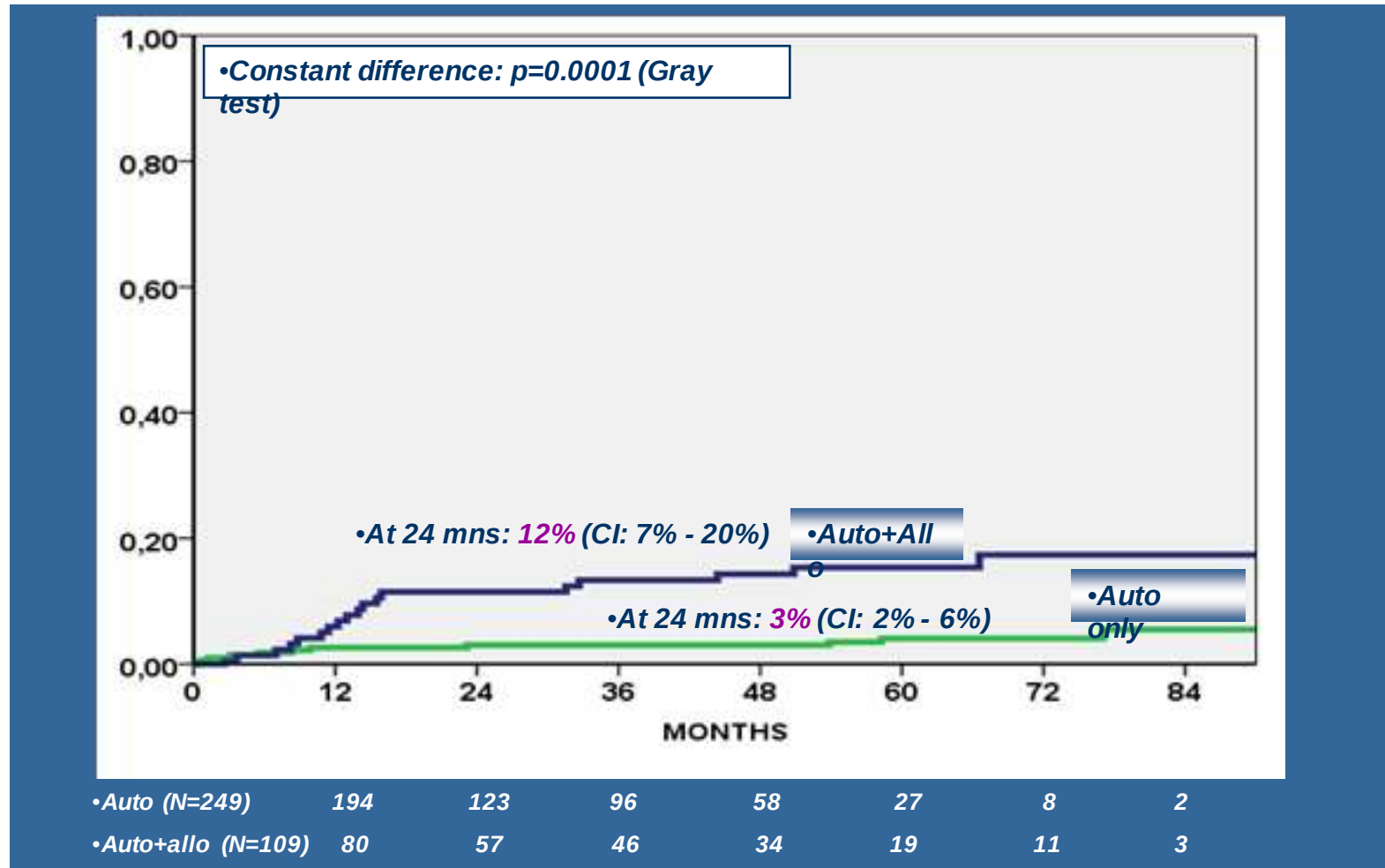
Progression-free survival

Tandem autologous/reduced-intensity allogeneic stem cell transplantation versus autologous transplantation in myeloma – long term follow up.



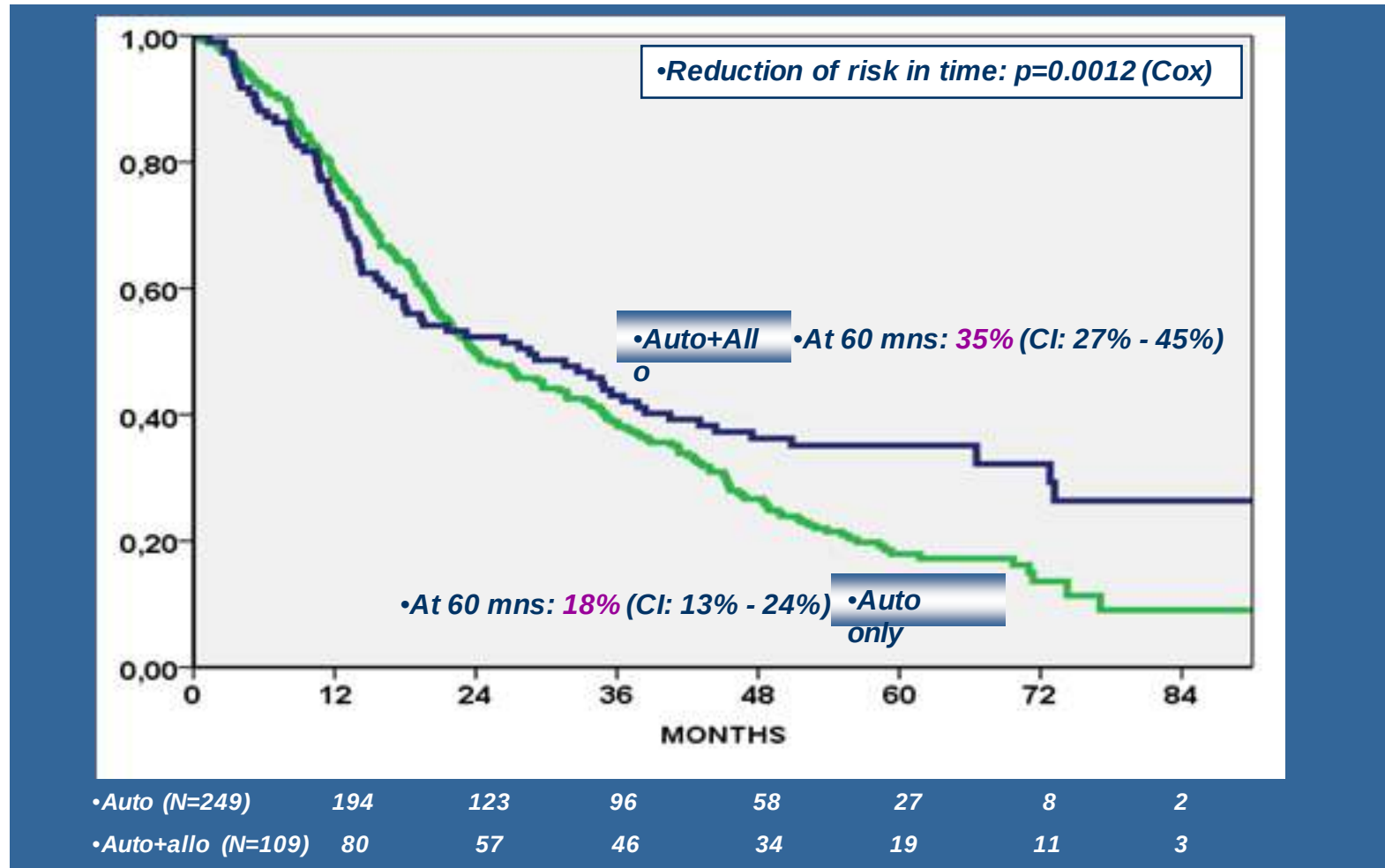
Auto/RIC-allo versus Auto in Myeloma

Non-Relapse Mortality since 1st transplant



Auto/RIC-allo versus Auto in Myeloma

Progression Free Survival since 1st transplant

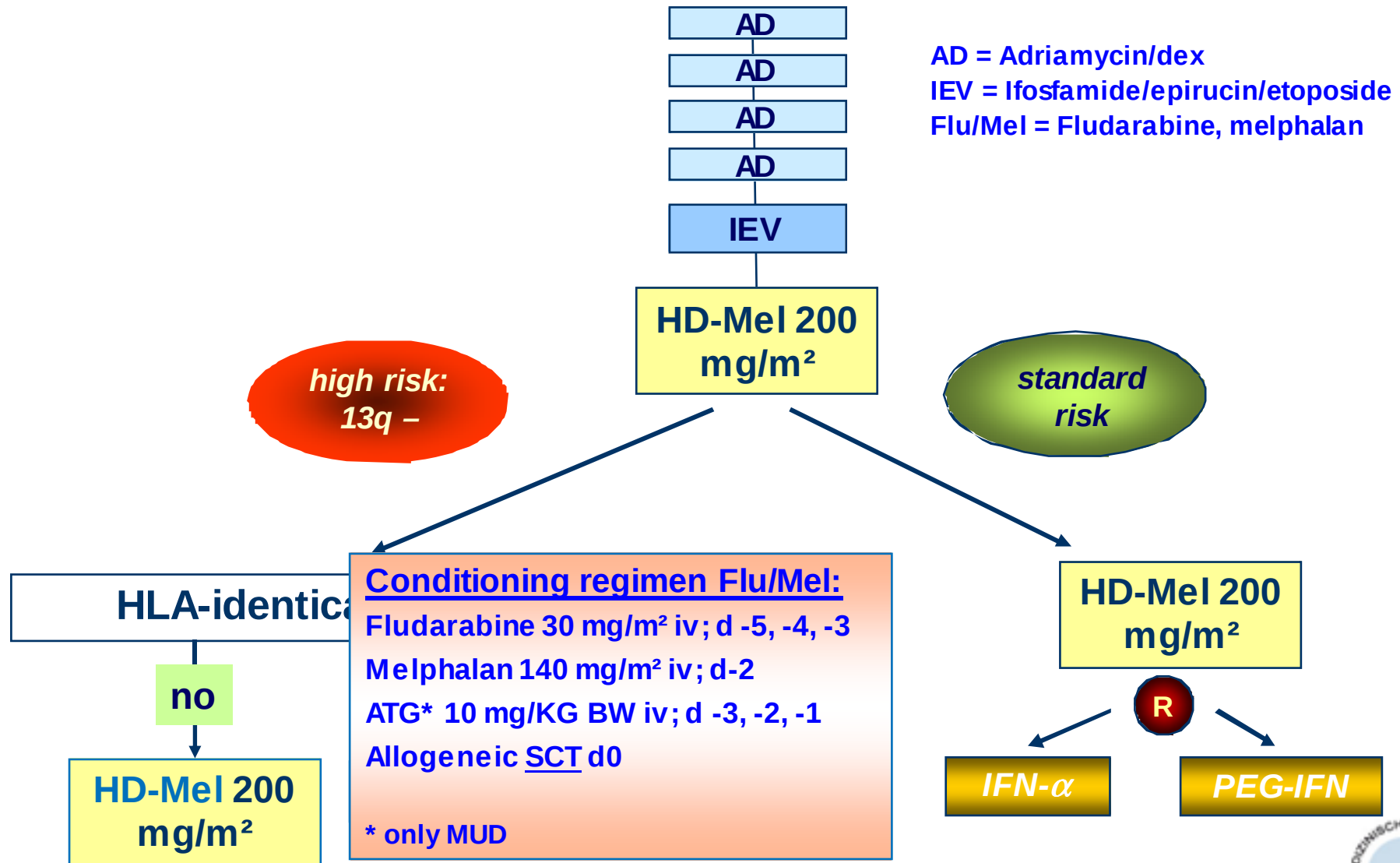


Tandem Autologous(ASCT) / Allogeneic Reduced Intensity Conditioning Transplantation (RIC) with Identical Sibling Donor Versus ASCT in Previously Untreated Multiple Myeloma (MM):

	Outcome (Med. Follow-up 60 mo.)		
	RIC-Allo (n=88)	Tandem-Auto (n=104)	p
CR rate	51%	43%	n.s.
5 yrs Progression Rate	45%	77%	p<0.05
5 yrs PFS	35%	18%	P=0.001
Subgroup del13	31%	11%	P=0.002
5 yrs OS	63%	60%	n.s.
Subgroup del13	70%	53%	n.s.

Risk-stratified DSMM V trial

Enrolment into high-risk group, n = 199



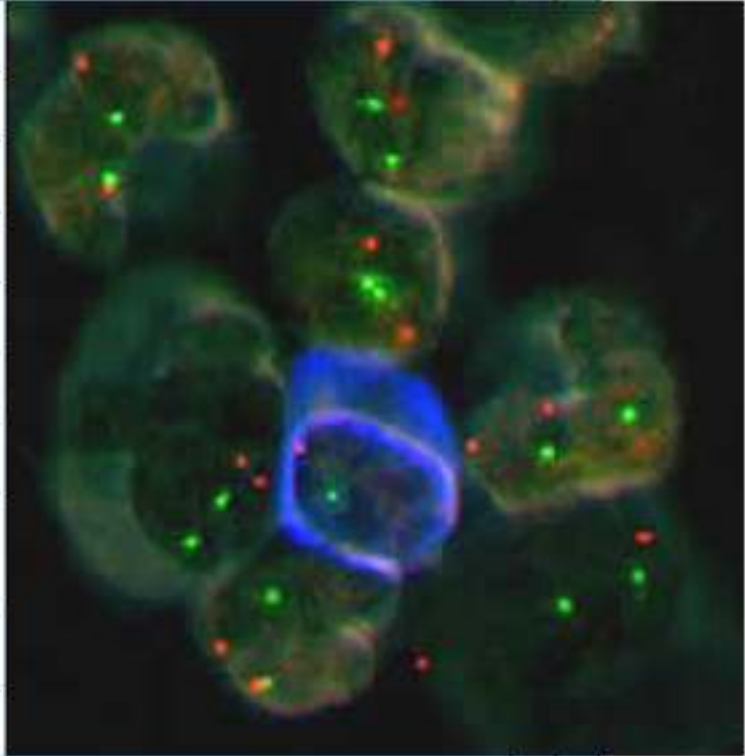
Patient characteristics

Subjects positive for del13q14 on central molecular cytogenetics

Variable	Tandem-Mel n=73	Auto/allo-SCT n=126
Median age (range) [years]	56 (30-60)	52 (34-60)
Gender distribution (female/male) [%]	45/55	48/52
Durie&Salmon Stages [%]		
- II	25.1	19.8
- III	75.3	80.2
Type of MM [n (%)]		
- IgG	39 (53.4)	61 (48.4)
- IgA	18 (24.7)	36 (28.6)
- Light chain	15 (20.6)	28 (22.2)
- Not known	1 (1.4)	1 (0.8)
LDH > Upper limit of normal [%]	20.0	19.5
Elevated serum creatinine [%]	24.7	22.2
Median serum β -2-microglobulin, (range) [g/dl]	3.3 (0.6-10.5)	2.9 (0.3-32.0)

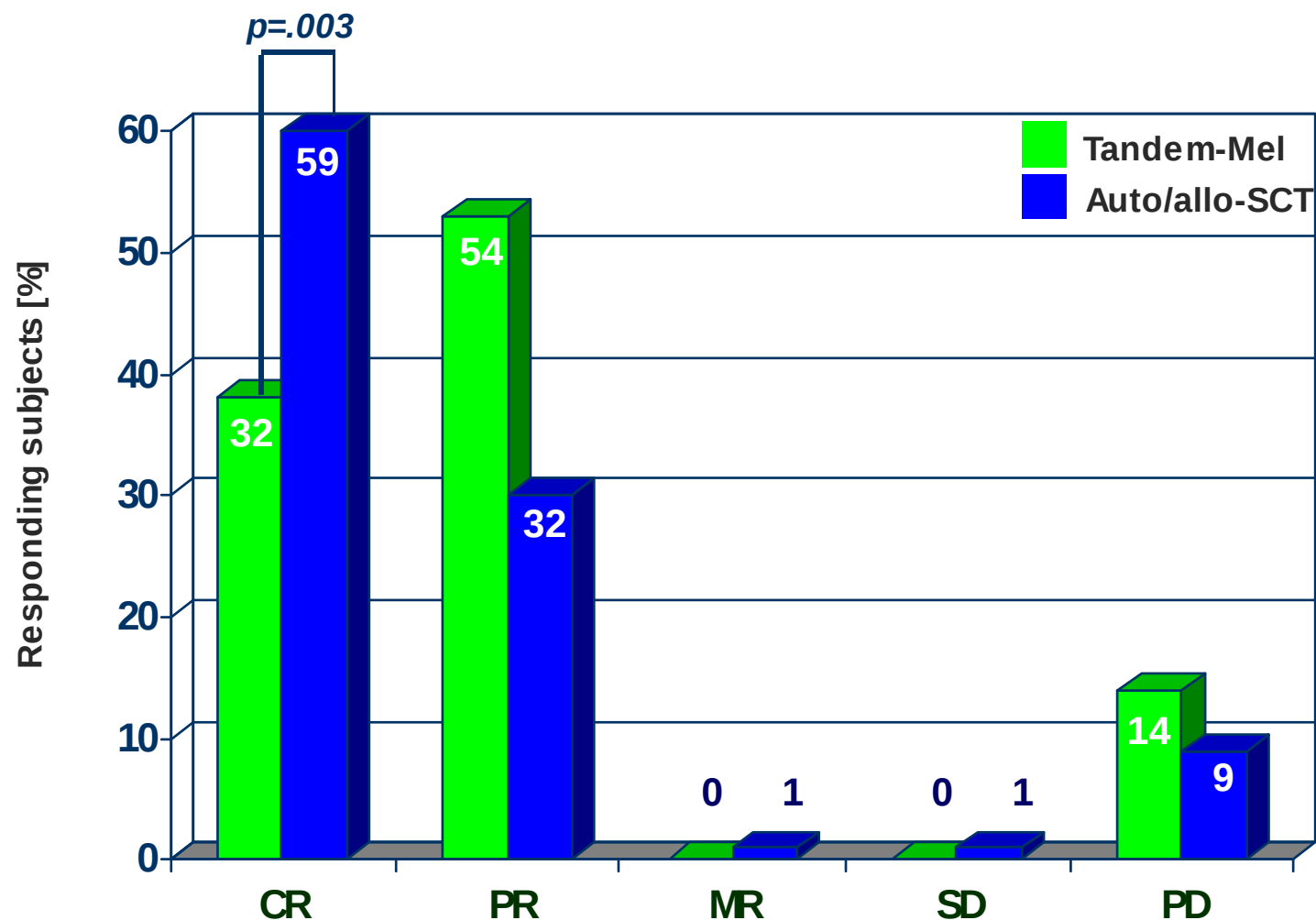
Central cytogenetic analysis for all patients in addition to del 13q (FISH)

Dr Peter Liebisch/Dr Christian Langer/Prof. Dr H. Döhner / Ulm

17p13 Deletion	
t (4;14) Translocation	
t (4;16) Translocation	
t (11;14) Translocation	
1q21.2 Gain	
11q22.3 Gain	
11q25 Gain	
22q11 Deletion	
1p22 Deletion	
9q34.2 Gain	

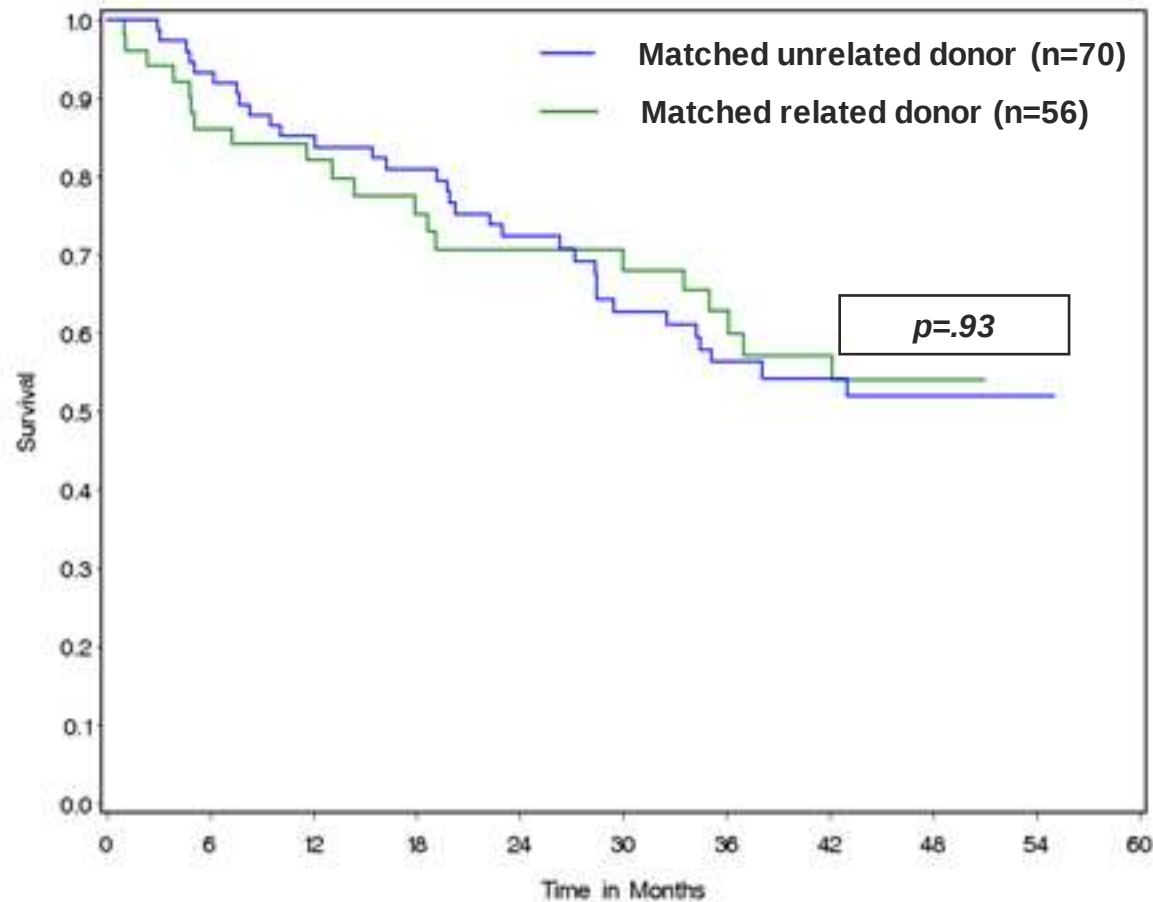
Response Rate/Quality in High Risk patients

Response 12 months after end of therapy according to treatment arm



High Risk Patients

Survival for subjects after auto/allo-SCT in relation to donor type



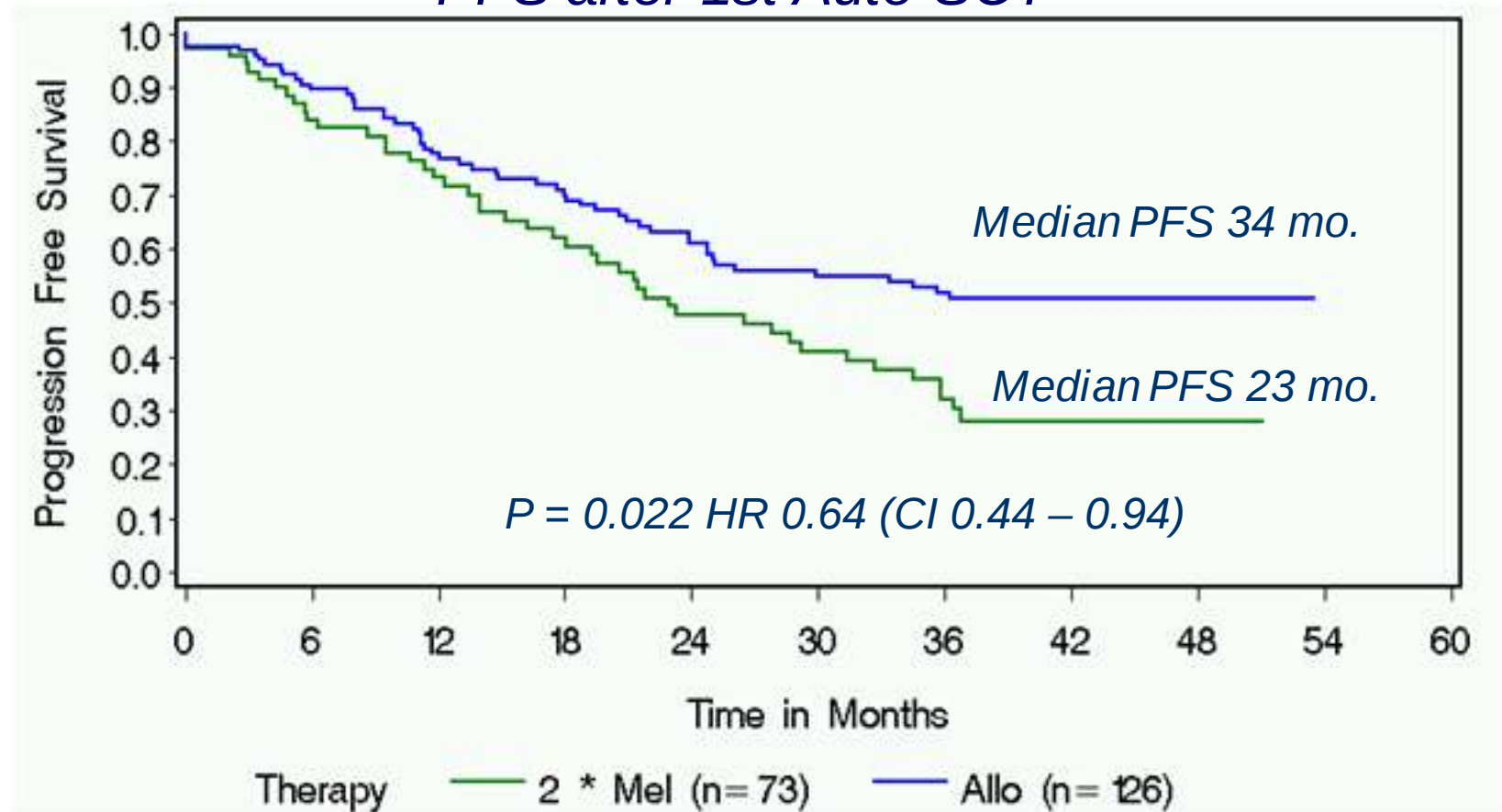
Treatment-related mortality for tandem-Mel at 2 years: 3/73 (4.1 %)

Treatment-related mortality for auto/allo-SCT at 2 years: 15/126 (11.9%)

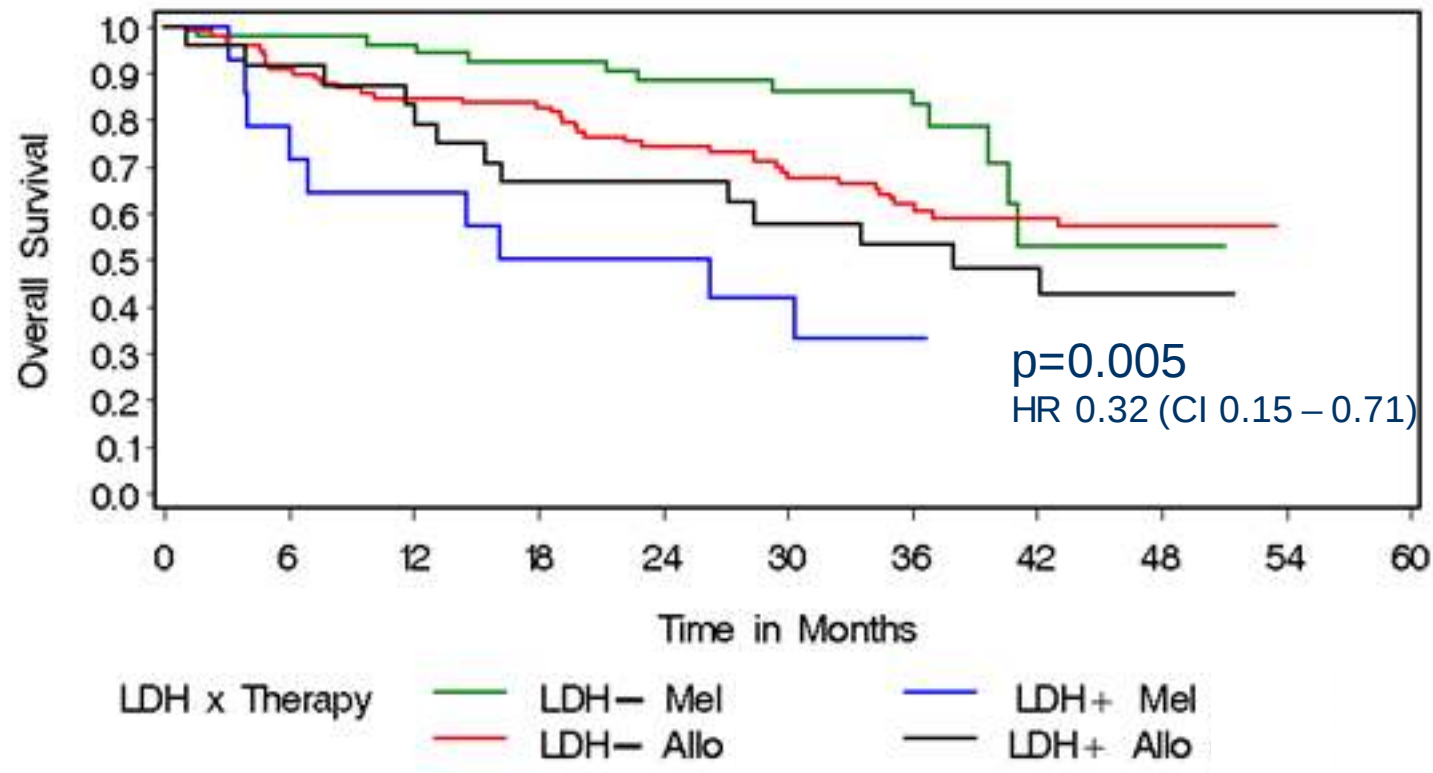
DSMM V Study High Risk Arm



PFS after 1st Auto-SCT

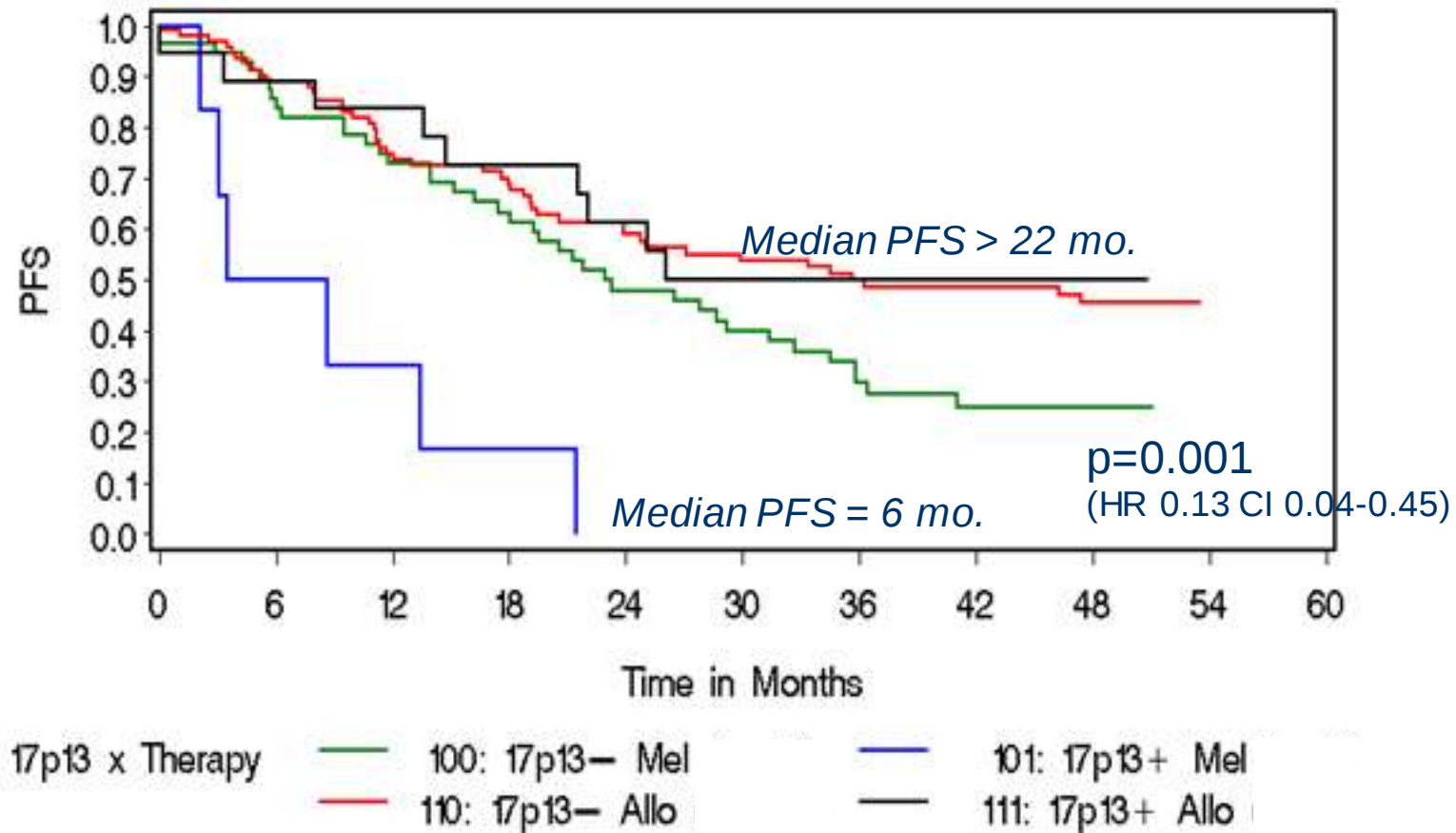


Patients with ü LDH benefit from Auto/Allo-SCT



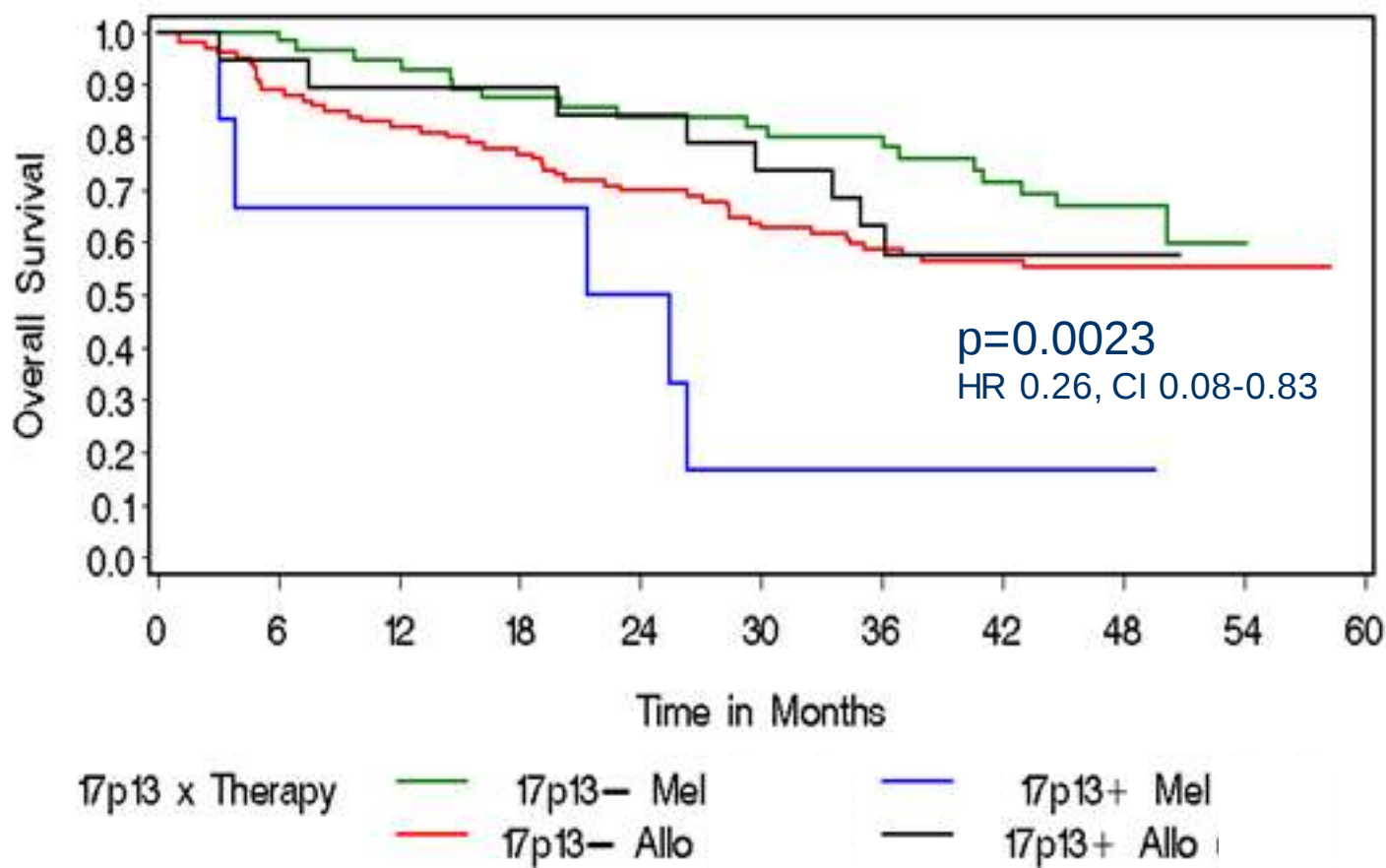
Kaplan-Meier-curves Study Arms C and D for PFS

Patients with a del 17p13 benefit from Auto/Allo-SCT



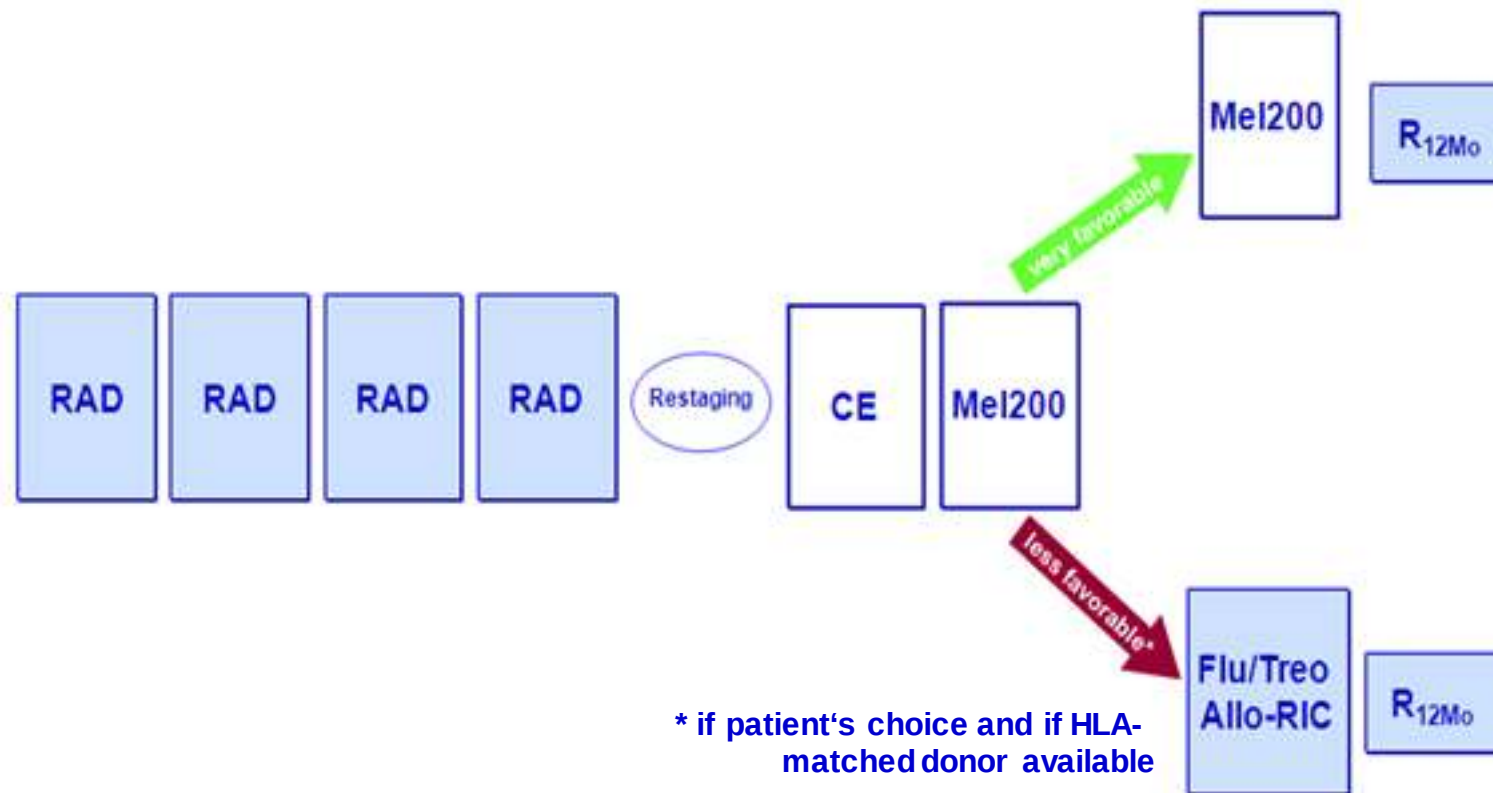
Kaplan-Meier-curves Study Arms C and D for PFS

Patients with 17p13-del benefit from Auto/Allo-SCT



Kaplan-Meier-curves Study Arms C and D for PFS

DSMM XII-Study



with 146 patients included
no therapy-related mortality

Conclusions

1. *Allogeneic SCT is a treatment option for high risk MM patients*
2. *Superiority of allogeneic SCT vs Auto-SCT in high risk patients demonstrated in 3/5 studies – number of high risk patients limited, no novel agents included in any of these studies*
3. *TRM after allografting for MM significant reduced*
4. *High relapse/progression rate also after allo-SCT*
 - *modulate GvM (vaccination/ adoptive cell therapy)*
 - *post-allo consolidation/maintenance*

Allogeneic Stem Cell Transplant versus Tandem High-Dose Melphalan for Front-Line Treatment of Deletion 13q14 Myeloma –

An Interim Analysis of the German DSMM V Trial

S Knop, P Liebisch, H Hebart, E Holler, M Engelhardt,
RC Bargou, B Metzner, D Peest, W Aulitzky, C Straka,
H Wandt, O Sezer, M Hentrich, H Ostermann, C Peschel,
G Hess, B Hertenstein, M Freund, M Kropff, HH Wolf,
W Jung, N Frickhofen, G Maschmeyer, HG Mergenthaler,
E Heidemann, N Kröger, C Engel, L Kanz, C Meisner, and H Einsele

... 50 dsmm centers

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Stefan Knop, MD, *Würzburg*

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Carmen Wesemeier, MD, *Würzburg*

Martina Haase, *Würzburg*

Mareike Vähröder, *Würzburg*

Martina Gropengießer, *Würzburg*

Biostatistics & data management

Christoph Meisner, PhD, *Tübingen*

Imma Fischer, PhD, *Tübingen*

Birgit Baumann, MD, *Tübingen*

dsmm –
doing studies on multiple
myeloma



Thank you for your attention!

