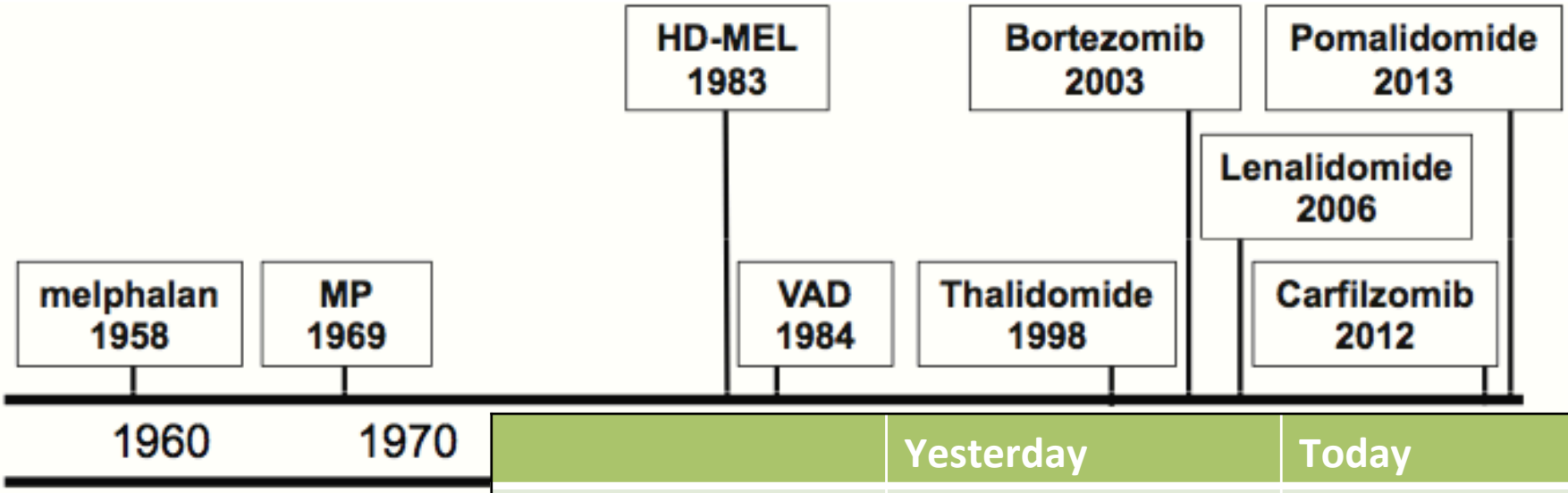
Azienda Ospedaliera – Universitaria
Ospedali Riuniti di Foggia

Autotrapianto singolo o doppio nel mieloma: è ancora lo standard?

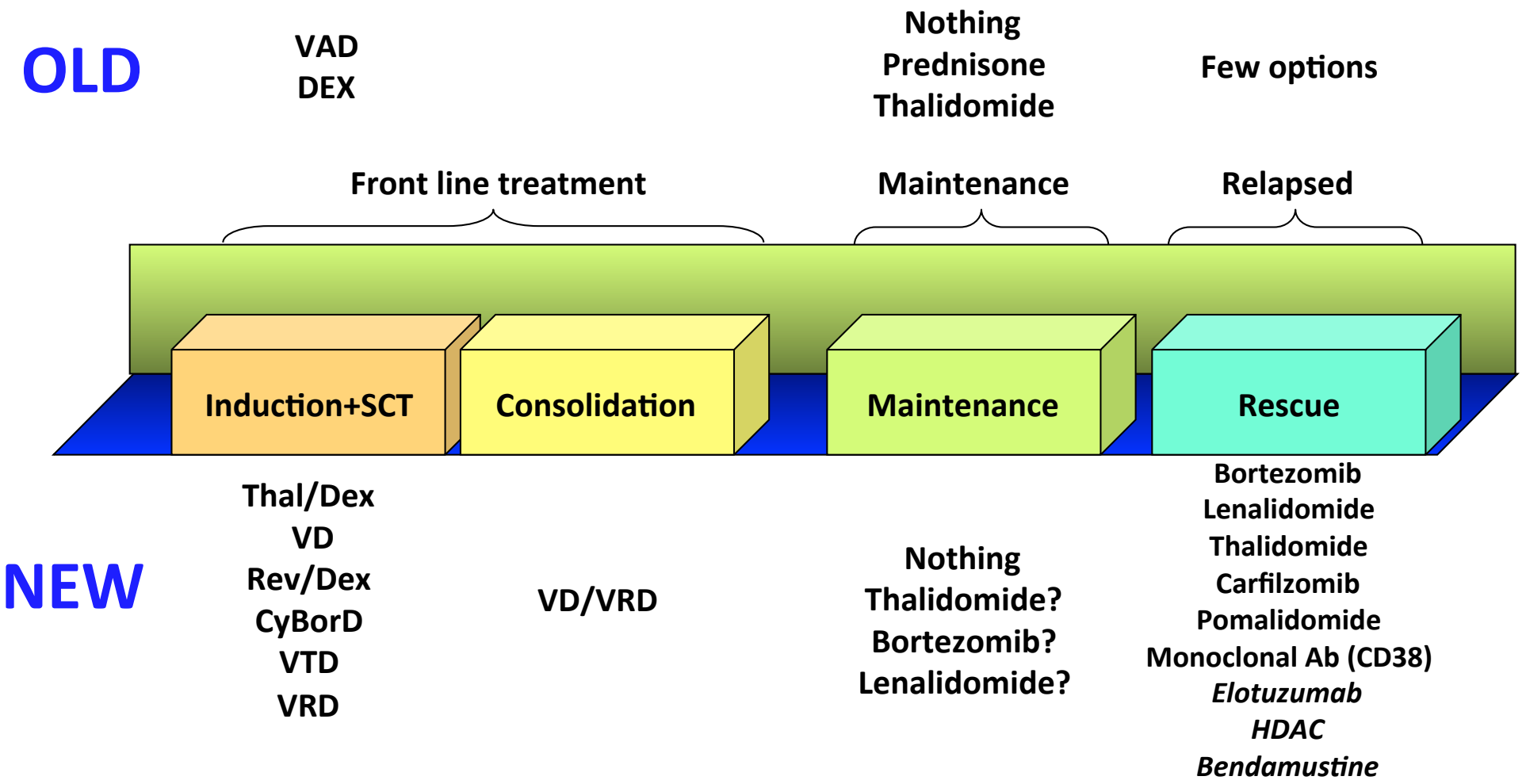
Silvana F. Capalbo
UOC Ematologia e Trapianto di Cellule Staminali Emopoietiche

Controversie nel Trapianto di Cellule Staminali Emopoietiche
BARI 6-7 Giugno 2017



	Yesterday	Today
Name	Multiple Myeloma	Myelomas
Staging System	Durie & Salmon	R-I.S.S.
Risk categories	B (RI); Cytogenetic (m-SMART)	MWG consensus ISS+LDH+CA+HR gene expression signature
Drugs	Old drugs	New drugs
Response Criteria	EBMT	IMWG criteria
Evaluation MRD	NO	Yes

Treatment sequence for patients eligible for SCT



Treatment of autologous stem cell- transplant-eligible multiple myeloma patients: ten questions and answers

1 Is high-dose therapy plus ASCT superior to conventional therapy?
2 Wath is the best induction treatment prior toASCT?
3 What is the optimal conditioning regimen prior to ASCT?
4 What is the best stem cell mobilization procedure prior to ASCT?
5 What is the impact of consolidation therapy after ASCT?
6 What is the impact of maintenance therapy after ASCT?
7 Which patients are candidates for ASCT?
8 Early vs late autologous ASCT in myeloma?
9 Single vs tandem transplant?
10 What is the role of ASCT as salvage therapy?

Mothy M et al. Haematologica 2014, 99(3): 408-416

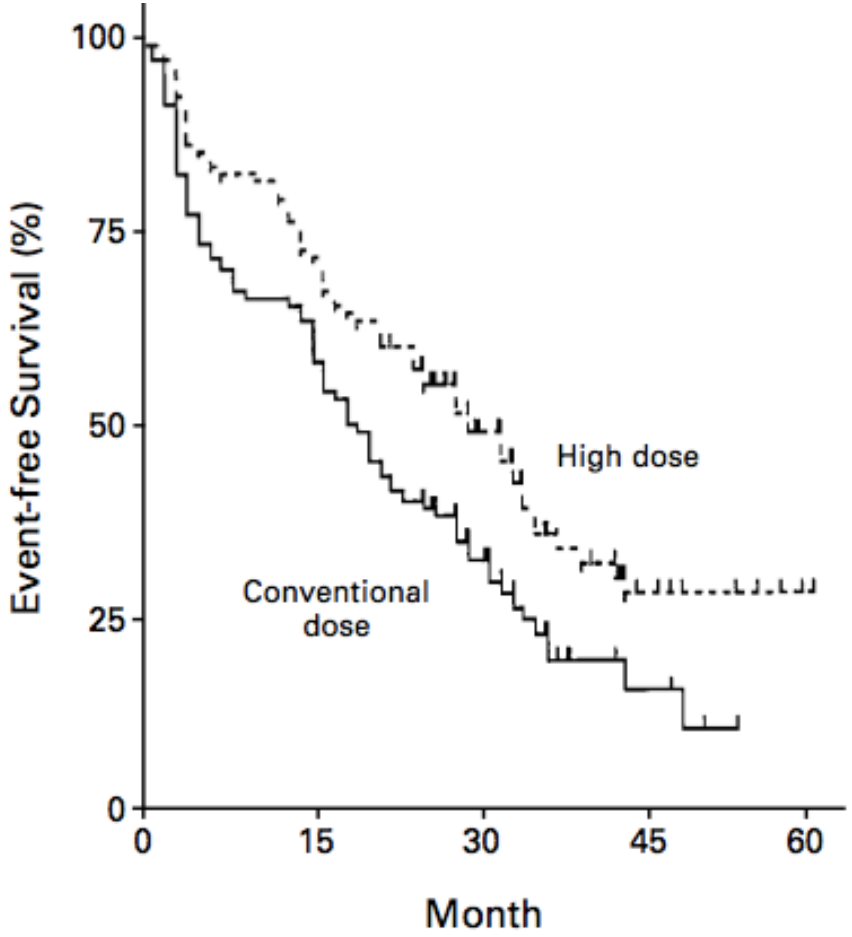
Questions

ASCT: transplant or not transplant

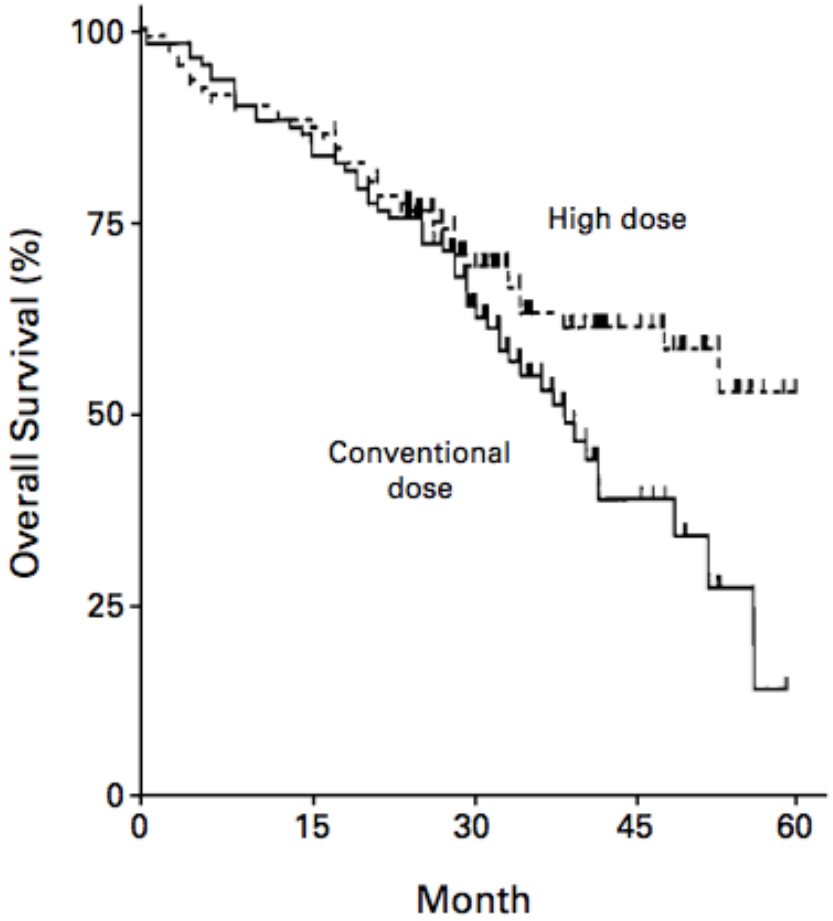
Single vs tandem ASCT

Second ASCT as salvage therapy?

A PROSPECTIVE, RANDOMIZED TRIAL OF AUTOLOGOUS BONE MARROW TRANSPLANTATION AND CHEMOTHERAPY IN MULTIPLE MYELOMA



Conventional dose	58 (48–68)	32 (23–42)	15 (7–28)	10 (3–27)
High dose	71 (61–79)	50 (39–55)	28 (18–40)	28 (18–40)



Conventional dose	63 (53–73)	35 (22–50)	12 (1–40)
High dose	69 (58–78)	61 (50–71)	52 (36–67)

IFM90
Induction regimen.: VMCP/BVAP
200 patients; ≥65 years age
II-III D&S

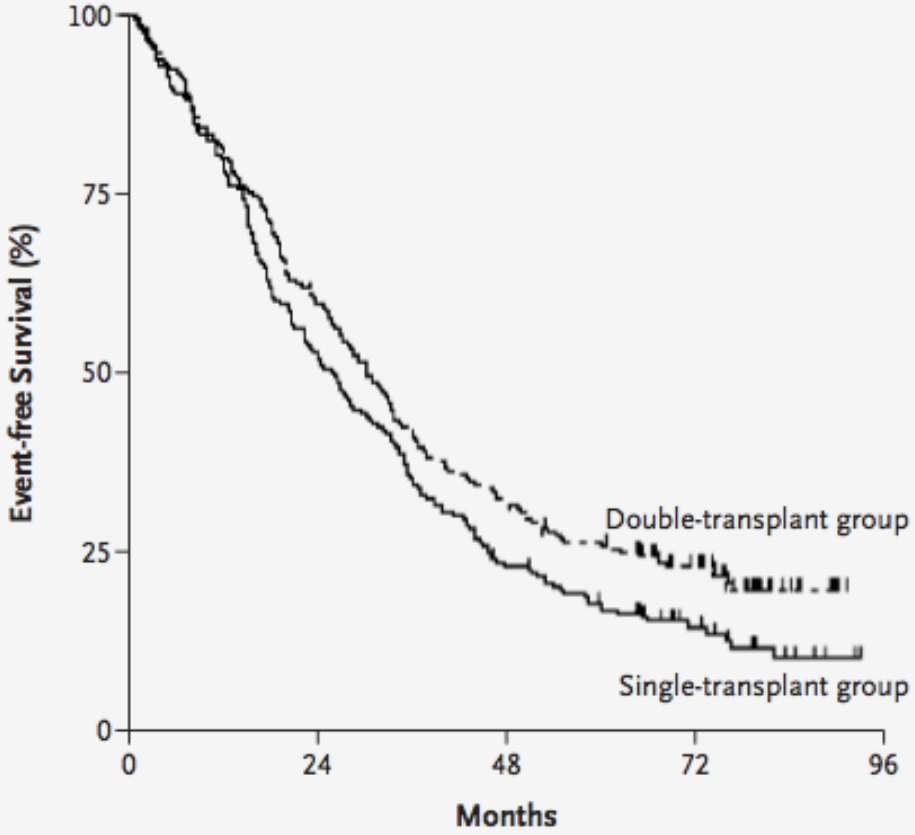
Attal et al N Engl J Med 1996; Jul 11, 335(2): 9-17

Summary of prospective randomized trials comparing conventional chemotherapy with ASCT

Author	Study Details	Response Data	PFS Data	OS Data
Child, 2003 [6]	Pts < 65 yr ABCM→IFN maintenance vs Dox-Methylpred-Cy → auto-HCT	CR 8% versus 44% favoring auto-HCT group ($P = .04$)	Favoring auto-HCT group ($P < .001$)	Favoring auto-HCT group ($P < .04$)
Blade, 2006 [7]	Pts < 65 yr VBMCP/VBAD→ 8 additional cycles versus auto-HCT (high dose Mel ± TBI)	CR 11% versus 30% favoring auto-HCT group ($P = .002$)	No difference	No difference
Fermand, 2005 [8]	Pts < 65 yr VMCP versus CHOP/VAMP→ auto-HCT with Mel versus Bu/Mel	*P* value not reported	EFS favoring auto-HCT group ($P = .07$)	No difference
Palumbo, 2004 [9]	Pts 50-70 yr MP × 6 versus Mel 100 mg/m^2 × 2	nCR = 6% versus 25% ($P = .002$)	EFS at 3 yr favoring auto-HCT group 16% versus 37% ($P < .001$)	OS at 3 yr favoring auto-HCT group 62% versus 77% ($P < .001$)
Barlogie, 2006 [10]	VAD→ VBMCP versus auto-HCT with Mel/TBI→ ± IFN maintenance	No difference	No difference	No difference
Palumbo, 2014 [11]	Len-Dex +Cy- mob→ MPR × 6 versus Mel 200 mg/m^2 auto-HCT × 2; all randomized to ± Len maintenance	*P* value not reported	Favoring auto-HCT group ($P < .001$)	Favoring auto-HCT group ($P < .02$)

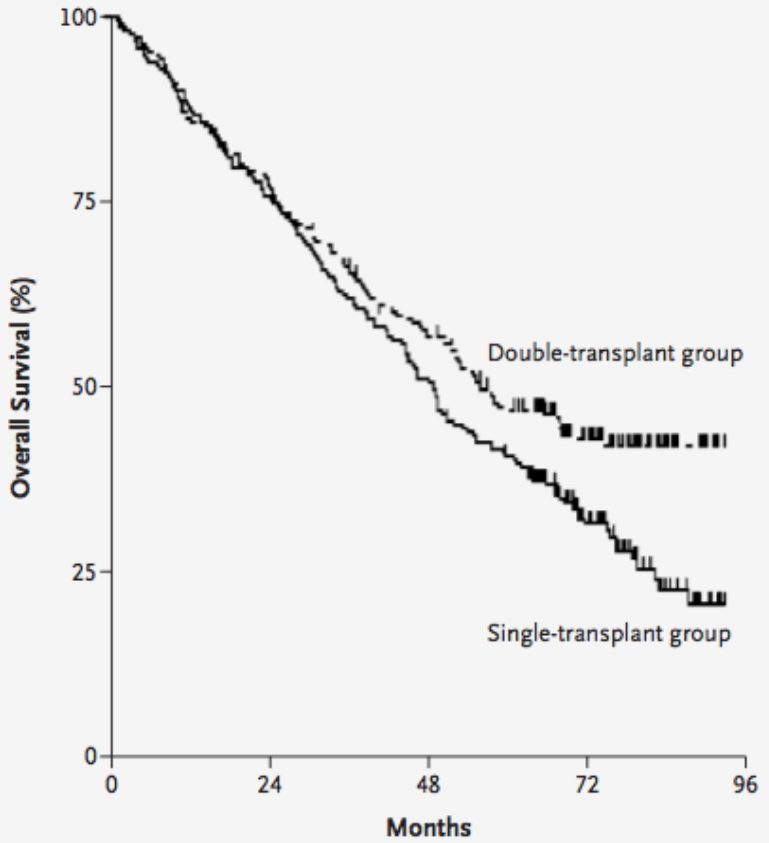
Shah et al. Biol Blood Marrow Transplant 2015; (21): 1155-66

Single versus Double Autologous Stem-Cell Transplantation for Multiple Myeloma



Probability of Event-free Survival (95% CI)

Single-transplant group	23 (17–29)	14 (10–20)	9 (5–15)
Double-transplant group	32 (26–38)	23 (17–28)	20 (14–26



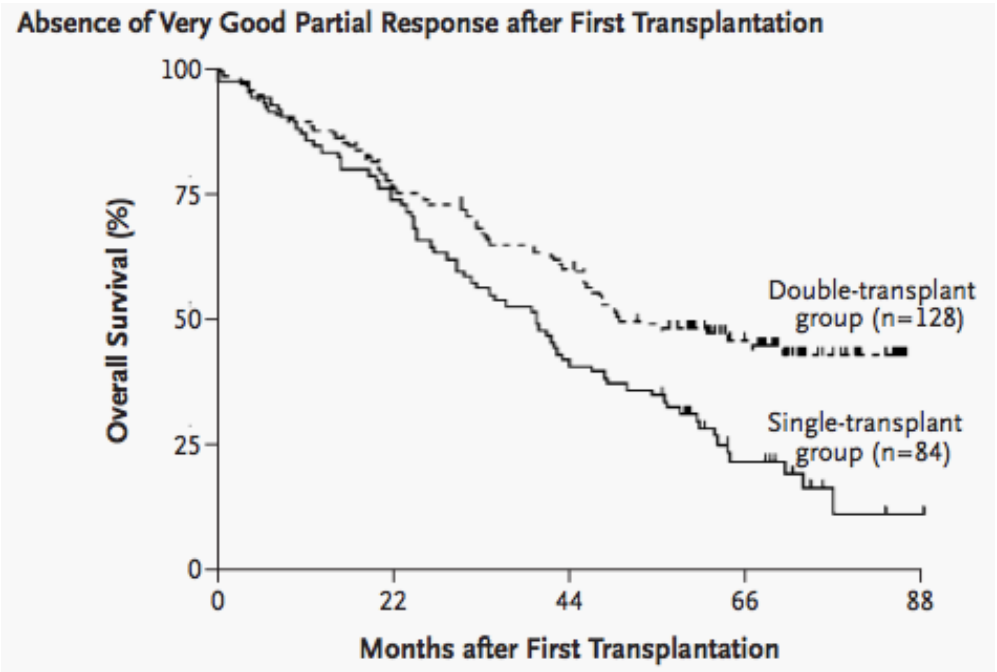
Probability of Overall Survival (95% CI)

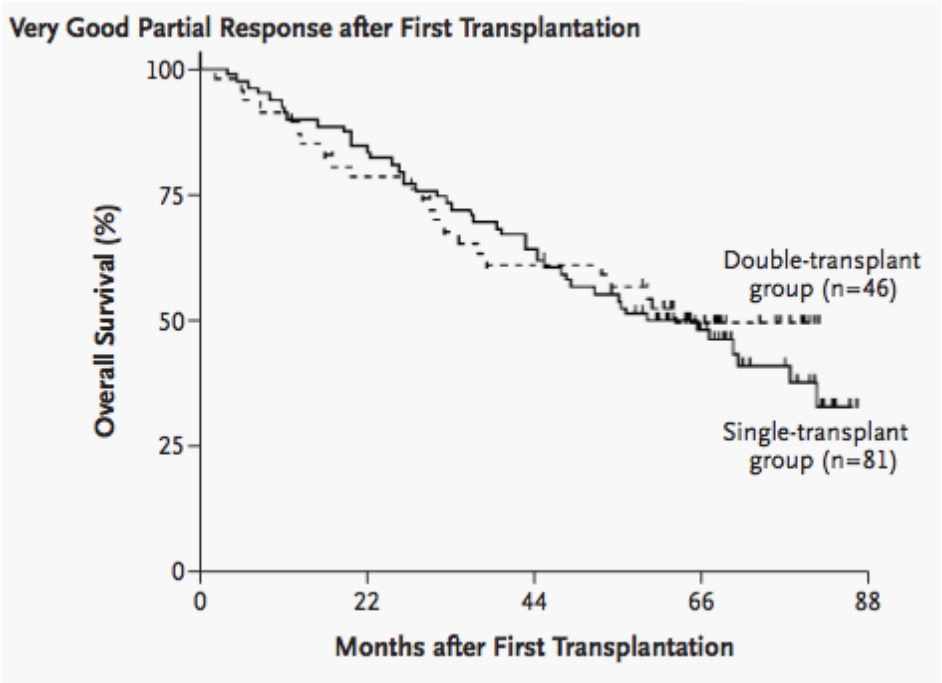
Single-transplant group	50 (43–57)	31 (24–38)	20 (13–29)
Double-transplant group	57 (49–64)	42 (35–50)	42 (34–49)

IFM94 trial
400 patients; <u>>60 years; I-II-III D&S</u>
Induction regimen: VAD (3)
Post-ASCT: IFNα x 10 months

Attal et al. N Engl J Med 2003 Dec25;349(26):2495-502

Single versus Double Autologous Stem-Cell Transplantation for Multiple Myeloma

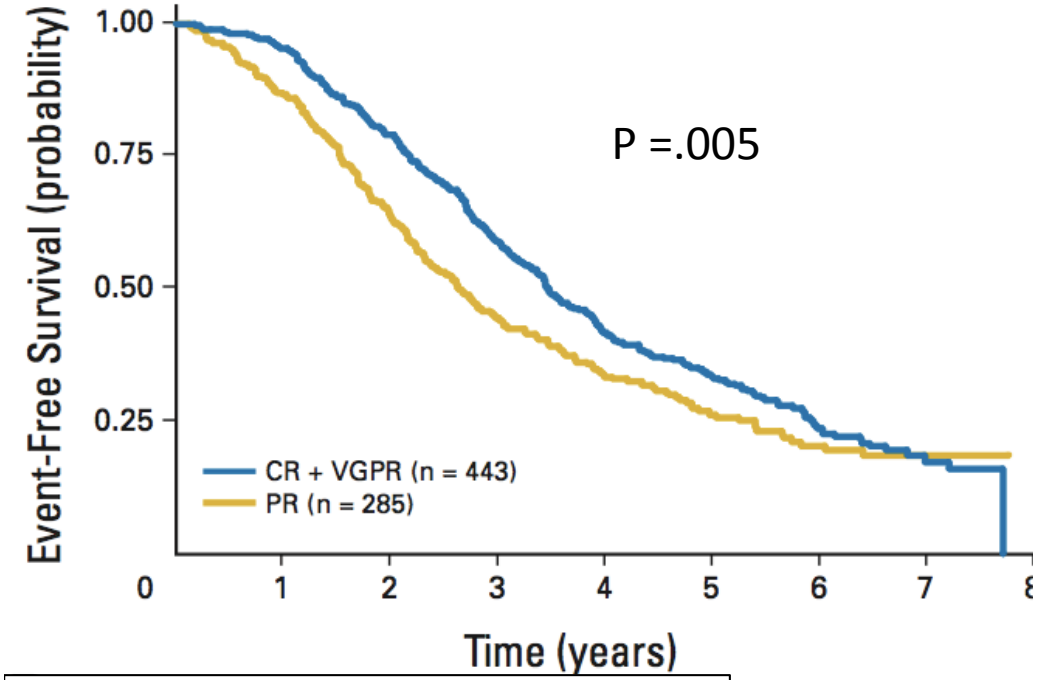


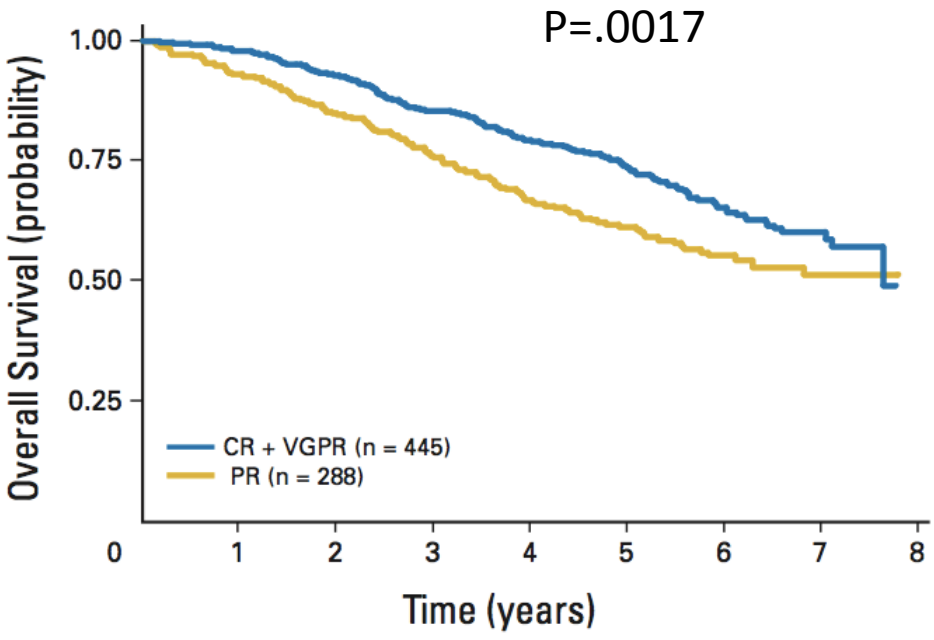


IFM94 trial
400 patients; <u>>60 years; I-II-III D&S</u>
Induction regimen: VAD (3)
Post-ASCT: IFNα x 10 months

Attal et al. N Engl J Med 2003 Dec25;349(26):2495-502

Achievement of at Least Very Good Partial Response Is a Simple and Robust Prognostic Factor in Patients With Multiple Myeloma Treated With High-Dose Therapy: Long-Term Analysis of the IFM 99-02 and 99-04 Trials



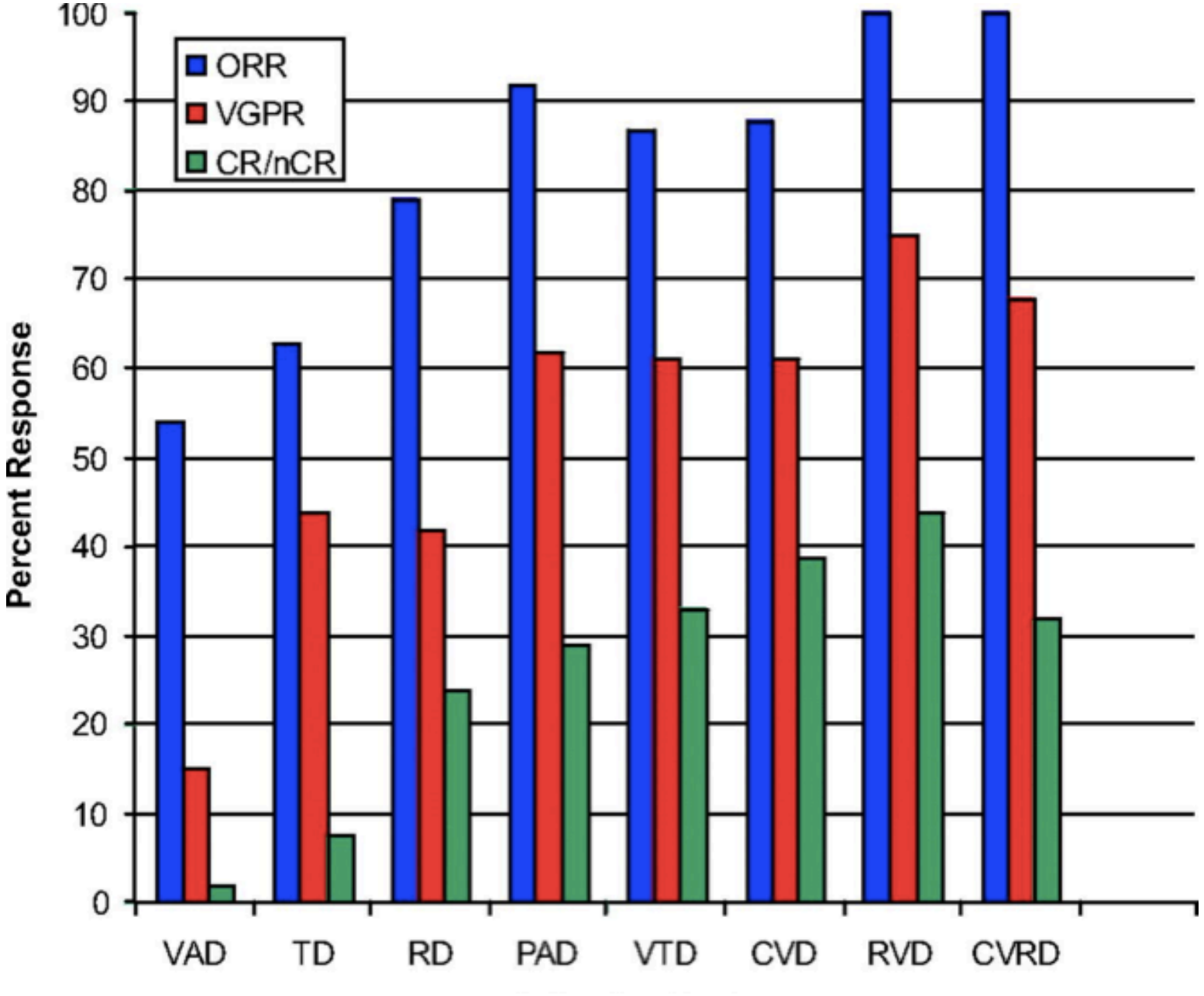


ISS:1-2-3
IFM99 02-04 (double transpalnt)
Induction regimen:VAD x3-4
CR+VGPR: 445 patients
PR: 228 patients;
Response: pre-EBMT criteria

Conclusion :In the context of ASCT, achievement of at least VGPR is a simple prognostic factorin term of EFS and OS that has importance in intermediate and high-risk MM and can be informative in more patients than CR.

Harousseau et al. J Clin Oncol Dec1:27(34):5720-6

Incorporation novel agents in the upfront treatment of MM to improve the CR/VGPR rate



Bortezomib Plus Dexamethasone Is Superior to Vincristine Plus Doxorubicin Plus Dexamethasone As Induction Treatment Prior to Autologous Stem-Cell Transplantation in Newly Diagnosed Multiple Myeloma: Results of the IFM 2005-01 Phase III Trial

482 patients

VAD; VAD + DCEP consolidation; VD; VD + DCEP followed by ASCT

Patients not achieving VGPR required a 2nd ASCT.

The primary end point was postinduction CR/nCR rate.

Response to Induction
Evaluable patients

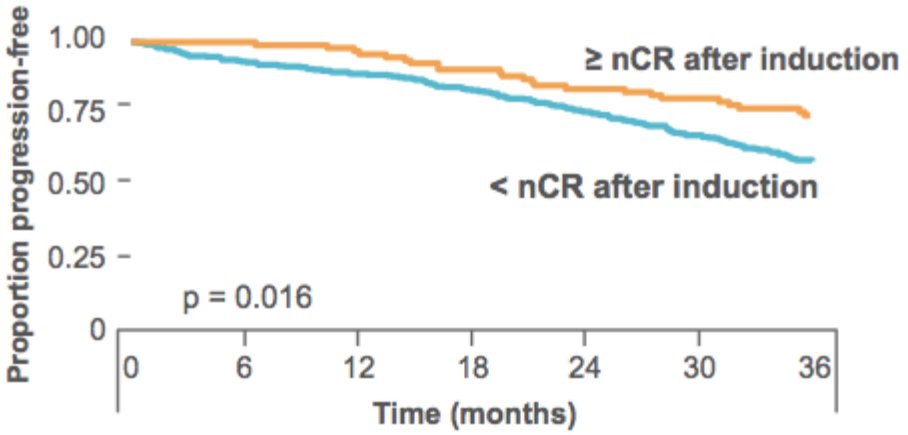
	VAD N=218	Vel-Dex N=223	P value
CR	1.4%	5.8%	0.012
CR+nCR	6.4%	14.8%	0.004
≥ VGPR	15.1%	37.7%	< 0.0001
≥ PR	62.8%	78.5%	.0003
MR+SD	26.6%	12.6%	
PD	4.1%	4.5%	
Death	2.8%	0.5%	

Response to 1° ASCT
Evaluable patients

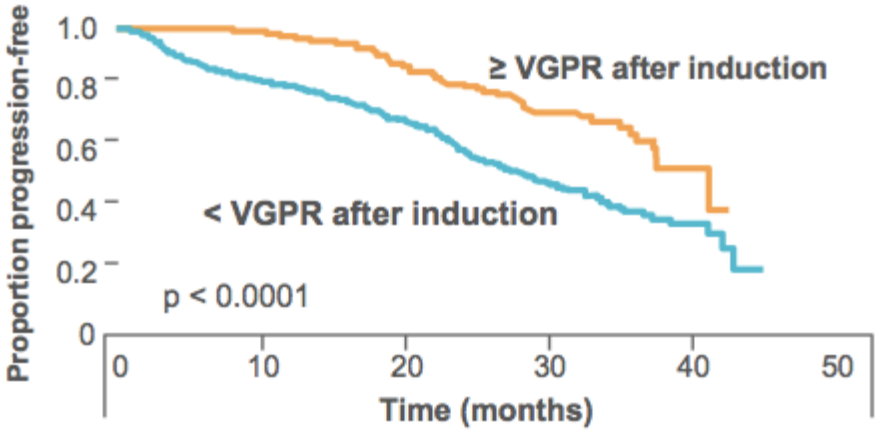
	VAD N=218	Vel-Dex N=223	P value
CR	8.7%	16.1%	0.016
CR + nCR	18.4%	35%	<0.001
≥ VGPR	37.2%	54.3%	<0.001
≥ PR	77.1%	80.3%	0.401
MR/SD/PD	3.7%	2.7%	
No ASCT	15.6%	11.7%	

Harousseau et al J Clin Oncology 2010 Oct 20; 28(30: 4621-9

Achievemen of high-quality response after induction therapy prognosticates for extended PFS after ASCT



Variable	HR (95% CI)	p value
Absence of t(4;14) ± del(17p)	0.51 (0.36–0.73)	< 0.0001
B2-m ≤ 3.5 mg/L	0.47 (0.33–0.67)	0.0020
Response to induction ≥ nCR	0.98 (0.97–0.99)	0.0187



Variable	RR (95% CI)	p value
t(4;14) ± del(17p)	1.5 (1.0–2.1)	0.0621
ISS stage 2 and 3	1.8 (1.4–2.4)	< 0.0001
Response to induction < VGPR	2.3 (1.6–3.2)	< 0.0001

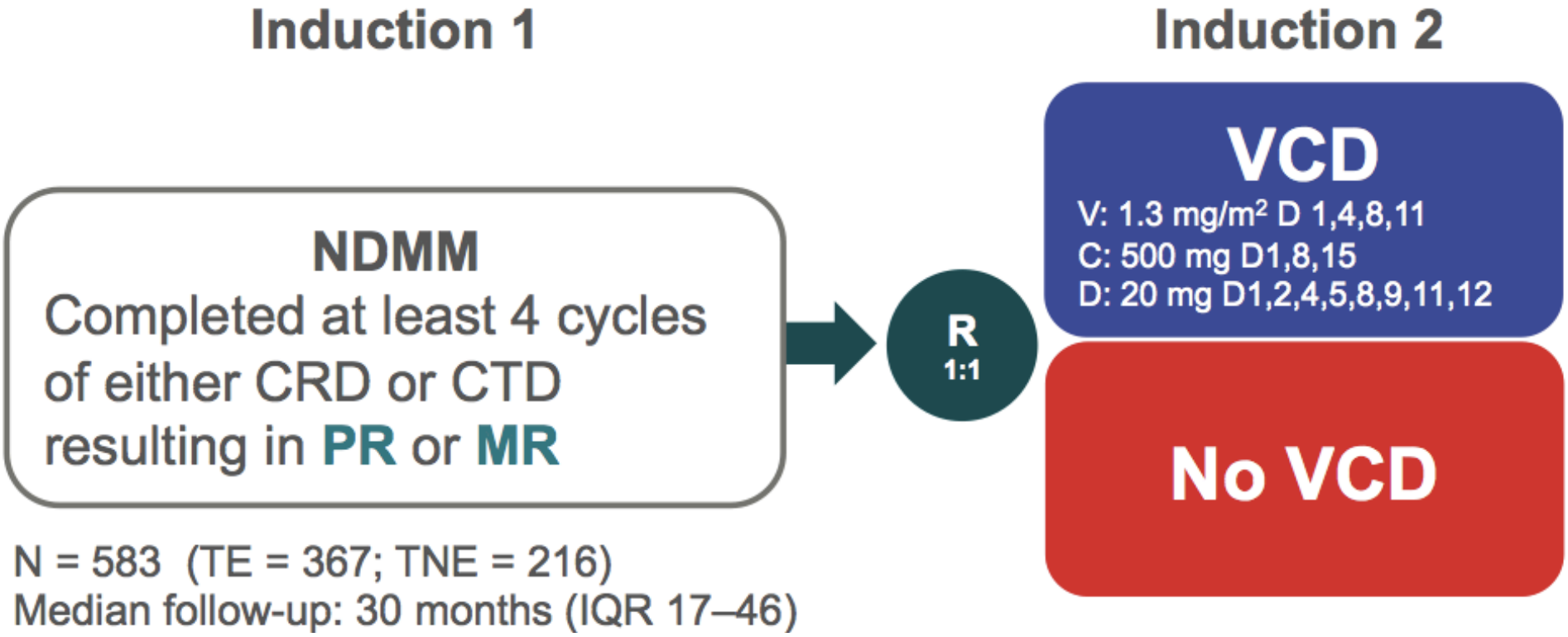
Cavo M, et al. Lancet. 2010;376:2075-85.

Moreau P, et al. Blood 2011;117:3041-4.

GIMEMA 26866138-MMY-3006
480 patients, ≤ 65 years
Induction:VTD +double ASCT vs
TD + double ASCT
Consolidation: VTD vs TD
Primary endpoint: post-induction CR/nCR rate

IFM 2007 – 02
199 patients; ≤ 65 years
VD + 1 ASCT vs vTD +1 ASCT
Consolidation and maintenance at ph. Discrection
Primary endpoint: post-induction CR rate

Response adapted induction therapy: Myeloma XI phase 3 trial



N = 583 (TE = 367; TNE = 216)
Median follow-up: 30 months (IQR 17–46)

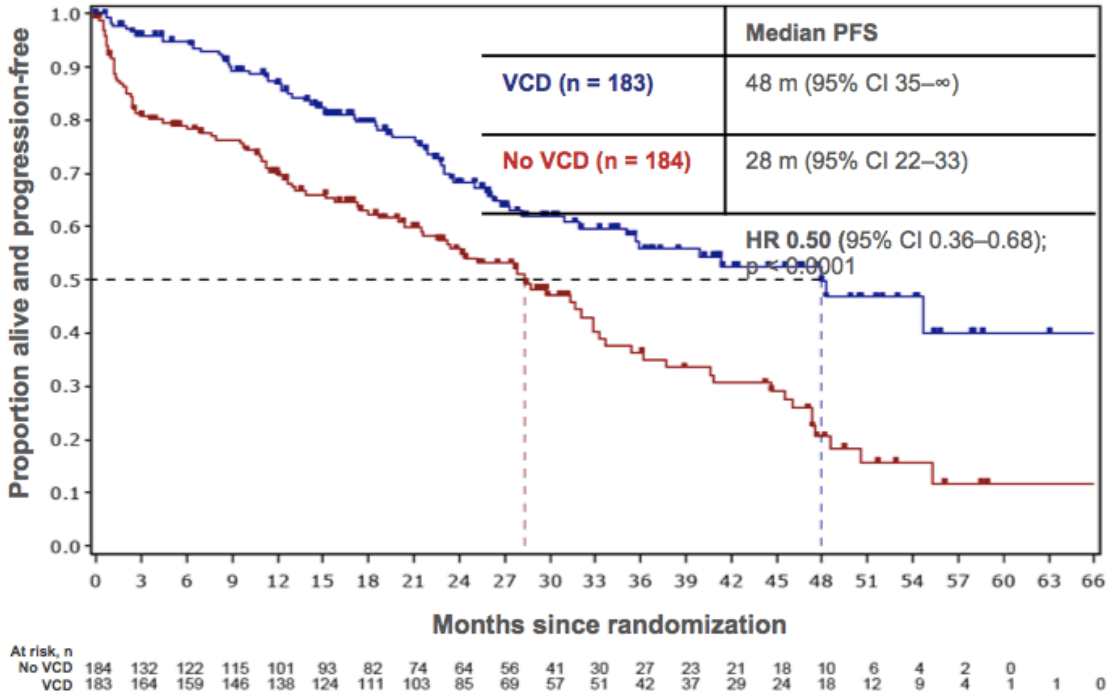
Exclusion criteria:
Patients were ineligible for the VCD randomization if they achieved a CR or VGPR or had PD or SD to induction (all primary refractory patients received VCD).

Primary endpoint: PFS and OS
Secondary endpoint.:Upgrading response
And PI impact in high-risk group

Jackson GH et al. Blood 2016; 128 Abst. 244 ASH

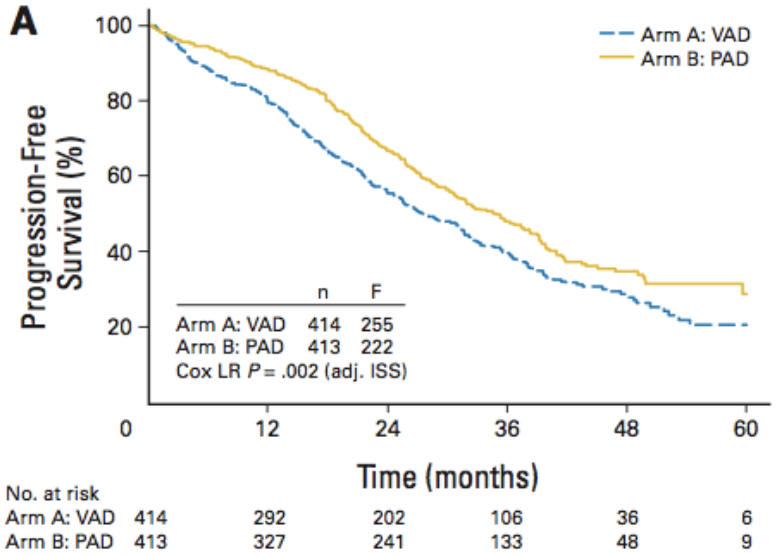
Salvage VCD induction vs no VCD in Myeloma XI: transplant-eligible patway

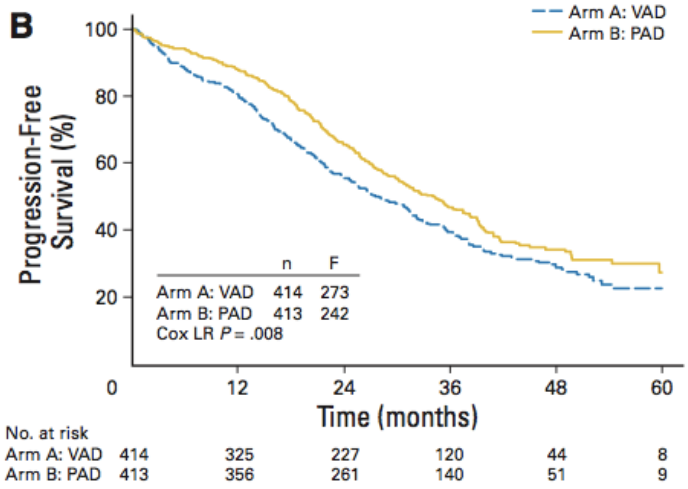
- Significant **improvement in PFS from 28 to 48 months for patients receiving VCD** (HR 0.50)
- **38% response improvement to ≥ VGPR with VCD**
- Response improvement after ASCT
  - VGPR/CR response: **65%** for patients receiving VCD vs **38%** for those who went straight to transplant

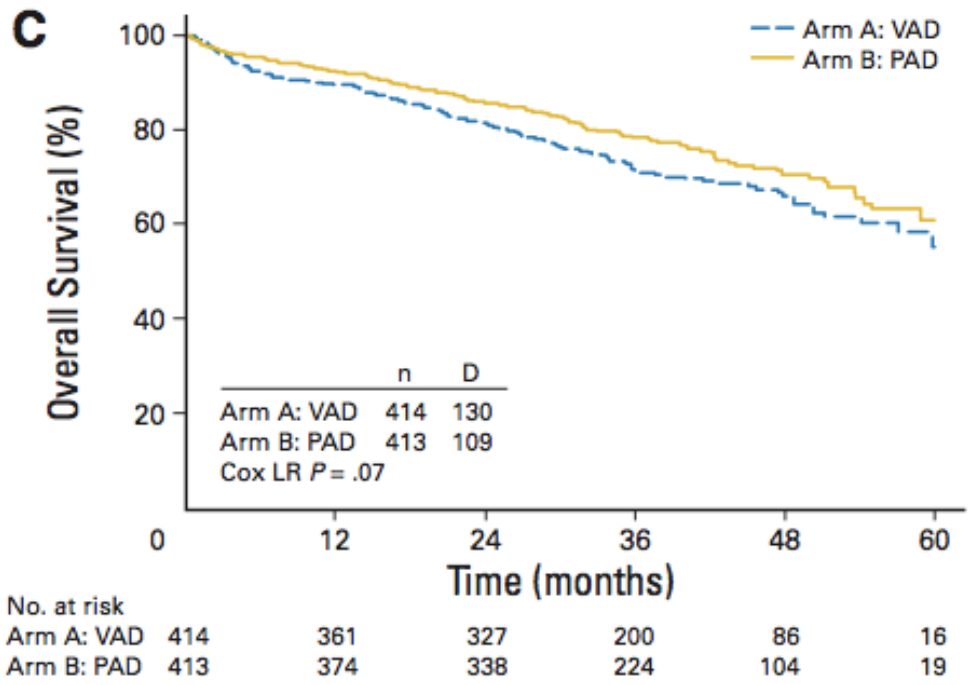


Jackson GH et al. Blood 2016; 128 Abst. 244 ASH

Bortezomib Induction and Maintenance Treatment in Patients With Newly Diagnosed Multiple Myeloma: Results of the Randomized Phase III HOVON-65/ GMMG-HD4 Trial







Patients: 827
ISS
Induction treatment: VAD vs PAD
Followed by 2 ASCT; RIC allo-SCT
Maintenance: Thalidomide vs Bortezomib

Sonneveld p et al. J Cl Oncol 2012; 2496-2955

Summary of randomized trials : Novel agent induction followed by ASCT

Trial	Induction	ASCT	VGPR Rate	Median PFS	OS
IFM 2005	VD vs. VAD	1 or 2 ASCT	VAD – 37%	30 mo	77% at 3 yrs
			VD – 54%	36 mo	81% at 3 yrs
GMMG-HOVON	VAD vs. PAD	1 or 2	VAD- 61%	42% @ 3 yrs	71% @ 3 yrs
			PAD- 75%	48% @ 3 yrs	78% @ 3 yrs
IFM 2007	VD vs. vTD	1 or 2	VD – 59%	Not reported yet	
			vTD - 73%		
GIMEMA	TD vs. VTD	2	TD – 69%	75% @ 2 yrs	91% @ 2 yrs
			VTD – 87%	85% @ 2 yrs	96% @ 2 yrs

Studies examining Single vs Tandem Auto-HCT

Author	Conditioning Regimen	TRM/ORR	EFS	OS
Attal, 2003 [46]	TBI 8 Gy and Mel 140 mg/m^2 versus Mel 140 mg/m^2 followed by TBI 8 Gy and Mel 140 mg/m^2; IFN maintenance offered to all pts	TRM 4% versus 6% ORR 84% versus 88%	Favoring tandem arm; 25 mo versus 36 mo (P = .03)	Favoring tandem arm 48 versus 58 mo (P = .01)
Cavo, 2007 [47]	Mel 200 mg/m^2 d-2 versus Mel 200 mg/m^2 followed by Mel 140 mg/m^2 d-2 and Bu 1 mg/kg PO × 12 d-5-to -3; maintenance IFN offered to all pts	TRM 3% versus 4% ORR NS CR + nCR 33% versus 47% (P = .01)	Favoring tandem arm; 23 versus 35 mo (P = .001)	65 mo versus 71 mo (P = .9)
Sonnevold, 2007 [48]	Mel 70 mg/m^2 i.v. × 2 versus Mel 70 mg/m^2 i.v. × 2; Cy 120 mg/kg i.v. and TBI 9 Gy; maintenance IFN offered to all pts	TRM not stated; ORR 88% for entire group CR 13% versus 32%	Favoring tandem arm; 21 mo versus 22 mo (P = .013)	55 mo versus 50 mo (P = .51)

Novel agent-based induction regimen

Phase 2 and 3 studies of thalidomide-dexamethasone and triplet thalidomide-based combinations in preparation for ASCT

		After induction		After ASCT			
Regimen	**N**	**CR + PR, %**	**CR/ ≥ VGPR, %**	**CR + PR, %**	**CR/ ≥ VGPR, %**	**PFS**	**OS**
TD vs	100	76	10/19	NR	NR	NR	NR
VAD (retrospective case-matched study)	100	52	8/14	NR	NR	NR	NR
TD vs	103	63	4/NR	NR	NR	NR	NR
VAD	104	41	0/NR	NR	NR	NR	NR
TD vs	100	66	NR/35	68	NR/44	NR	NR
Descamethasone	104	52	NR/13	62	NR/42	NR	NR
TAD vs	268	71	3/37	84	14/54	median, 34 mo	median, 73 mo
VAD	268	57	2/18	76	12/44	median, 22 mo	median, 60 mo
						$P < .001$	$P = .77$
CTD vs	NR	87	19/NR	NR	51/NR	NR	NR
CVAD	NR	75	9/NR	NR	40/NR	NR	NR
TT2 + THAL vs	323	NR	NR	NR	62/NR	5-yr, 56%	5-yr, 65%
TT2 without THAL	345	NR	NR	NR	43/NR	5-yr, 44%	5-yr, 65%
						$P = .01$	$P = .90$
Double ASCT + THAL vs	135	NR	NR/30	NR	NR/68	4-yr, 51%	5-yr, 69%
Double ASCT without THAL (retrospective case-matched study)	135	NR	NR/15	NR	NR/49	4-yr, 31%	5-yr, 53%
						$P = .001$	$P = .07$

NR: not reported

Cavo M et al. Blood 2011; 117:6063-73

Novel agent-based induction regimen

Phase 2 studies of bortezomib-based regimens in preparation for ASCT

Regimen	N	After induction		After transplantation		PFS, median	OS, 30 mo
		CR + PR, %	CR/ ≥ VGPR, %	CR + PR, %	CR / ≥ VGPR, %		
V (single agent)	64	41	NR (9)*/17	NR	NR	7 mo	30 mo, 79%
V ± D	32	87.5	6 (25)*/NR	NR	NR	NR	NR
VD	48	66	NR (21)*/31	90	NR (33)*/55	NR	NR
V alternated with D	40	65	12.5/22.5	88	33/55	NR	NR
PAD-1	21	95	24 (5)*/62	95	43 (14)*/81	median, 29 mo	2-yr, 95%
PAD-2	20	89	11 (5)*/42	90	37 (5)*/53	median, 24 mo	2-yr, 73%
VDD	50	78	NR (27)*/NR	93	27/NR	NR	NR
VDD	40	85	NR (37.5)*/57.5	87	NR (57)*/77	2-yr, 80%	2-yr, 92%
CyBorD	33	88	3 (39)*/61	NR	NR (70)*/74	NR	NR
VCD	391	85.4	NR (15)*/37	NR	NR	NR	NR
VTD vs VTDC	49 vs 48	100 vs 96	(29)/69 vs (31)/69	100 vs 100	(50)/87 vs (44)/85	NR	1-yr, 94.1% vs 94.2%
TT3 + VTD-PACE vs TT2 + THAL (retrospective comparison)	303 vs 323	NR vs NR	NR vs NR	NR vs NR	2-yr, 54/NR vs 51/NR	2-yr, 84% vs 77% (P = .008)	2-yr, 87% vs 83% (P = .12)

Cavo M et al. Blood 2011; 117:6063-73

Overview of VRD induction

Phase	Induction regimen	Cycles (n)	Post-induction response		Post-ASCT response	
			CR (%)	≥ VGPR (%)	CR (%)	≥ VGPR (%)
2	VRD[1]	8	37	74▲	NR	NR
2	VRD[2]	4	7	32	NR	NR
2	VRD[3]	3	23	58	47	70
3	VRD[4]	3	NR	50	NR	73

▲: Best Response
NR: Not Reported

1. *Richardson PG et al. Blood 2010; 116: 679-86*
2. *Kumar S et al Blood 2012; 119: 4375-82*
3. *Roussel M et al. J Clin Oncol 2014; 32: 2712-7*
4. *Attal M et al. ASH 2015 – N Engl J Med 2017; in press*

Lenalidomide, bortezomib and dexamethasone combination therapy in patients with newly diagnosed multiple myeloma (phase I/II study)

Best response to treatment for all patients and phase II population

	All patients (N = 66)			Phase 2 population (n = 35)		
Response*	**n**	**%**	**90% CI**	**n**	**%**	**90% CI**
CR	19	29	20-39	13	37	24-52
nCR	7	11	5-19	7	20	10-34
VGPR	18	27	18-38	6	17	8-31
PR	22	33	24-44	9	26	14-41
CR + nCR	26	39	29-50	20	57	42-71
CR + nCR + VGPR	44	67	56-76	26	74	59-86
At least PR	66	100	96-100	35	100	92-100

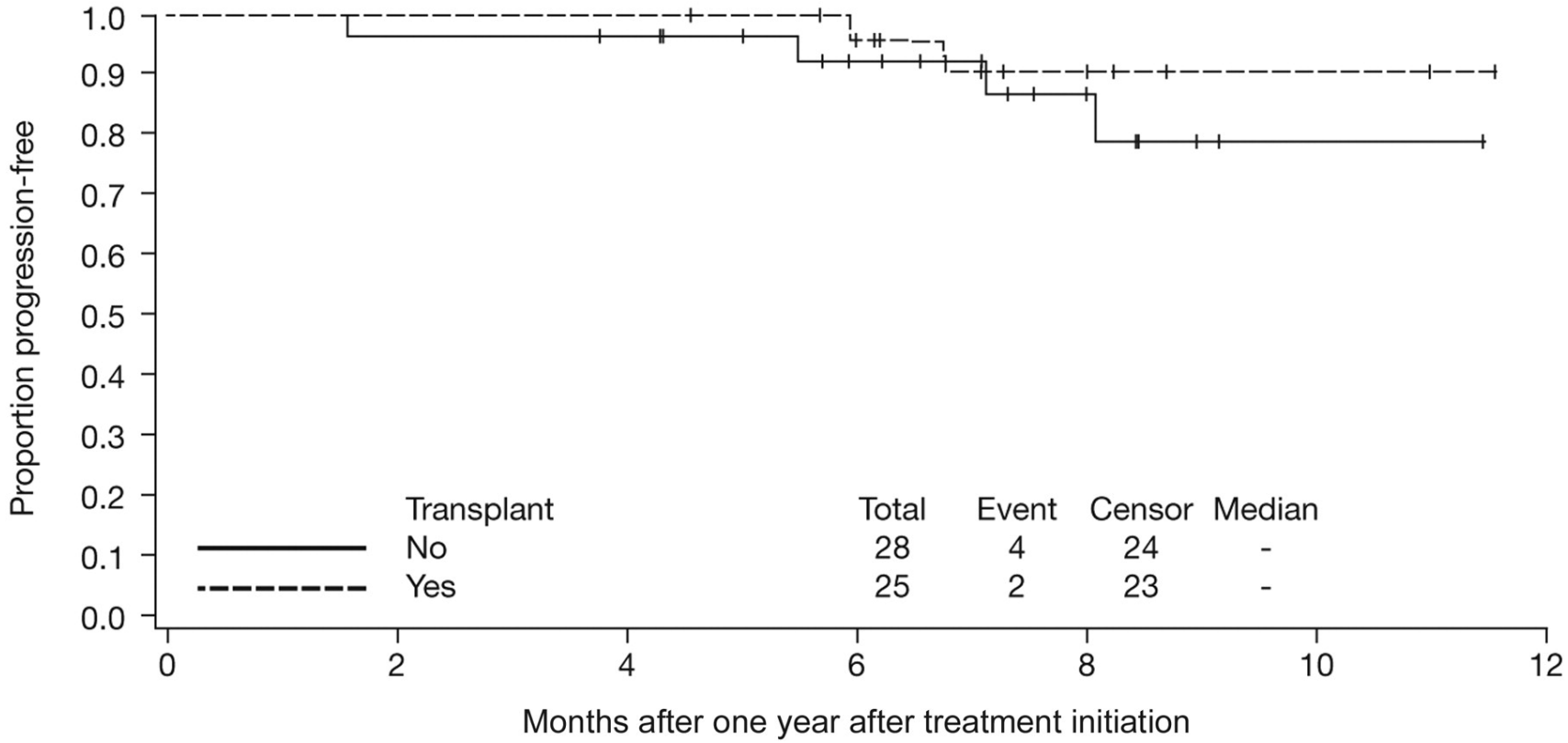
28 ASCT

Primary endpoints

- Phase I: MTD
- Phase II: PR or better

Richardson PG et al. Blood 2010; 116: 679-685

Kaplan-Meier estimate for PFS according to receipt of ASCT, from 1 year after treatment initiation.



Secondary end points:

- CrR + nCR
- Duration of R
- PFS
- OS

Paul G. Richardson et al. Blood 2010;116:679-686

blood

Hematopoietic Stem Cell Transplantation for Multiple Myeloma: Guidelines from the American Society for Blood and Marrow Transplantation

Shah et al. Biol Blood Marrow Transplant 2015; (21): 1155-66

Studies examining impact of cytogenetics on outcomes after Auto-HCT

Author	Cytogenetics/FISH Studied	Effect on PFS	Effect on OS
Falcon, 2001 [29]	Abnormality of 13 by FISH		Adverse prognostic factor ($P < .001$)
Chang, 2004 [30]	t(4:14)	Significantly worse ($P = .0003$)	Significantly worse ($P = .0001$)
Moreau, 2002 [31]	t(4:14)	EFS Significantly worse ($P < .000$)	Significantly worse ($P = .002$)
Chang, 2005 [32]	p53 deletion	Significantly worse ($P = .0324$)	Significantly worse ($P = .0008$)
Chang, 2010 [33]	Del 1p21	Significantly worse ($P < .001$)	Significantly worse ($P = .001$)
Avet-Loiseau, 2007 [34]	Composite FISH for del(13), t(11;14), t(4;14), hyperdiploidy, MYC translocations, and del(17p)	Adverse results for t(4;14), del(17p) (EFS)	Adverse results for t(4;14), del(17p) (EFS)
Fonseca, 2003 [35]	Composite of t(4;14), t(14; 16) and del17p		Significantly worse ($P < .001$)
Neben, 2010 [36]	Composite of t(4;14) and del17p with ISS II or III		Significantly worse ($P < .001$)

Prospective studies examinining preparative regimens for Auto-HCT in MM

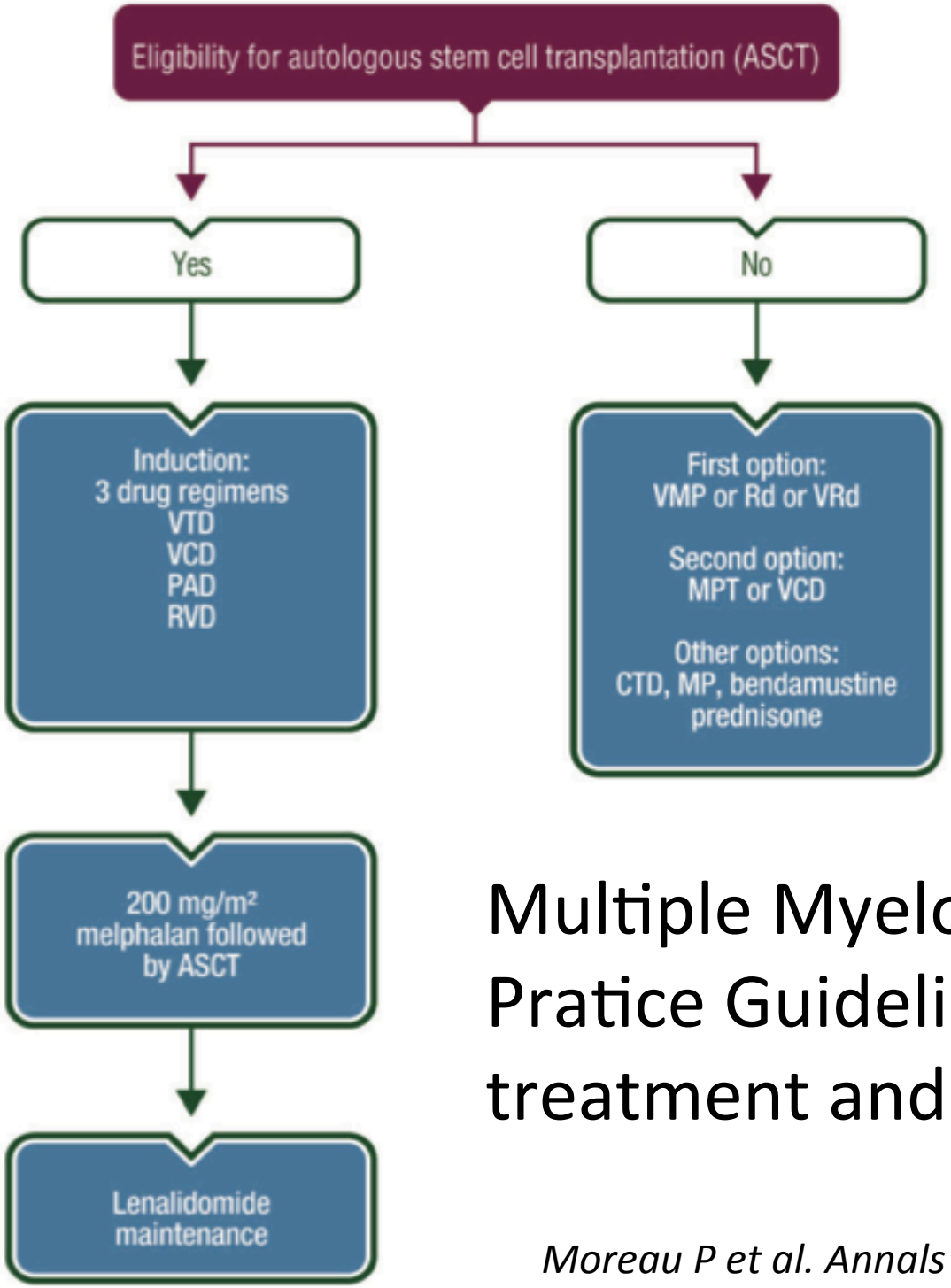
Author	Regimens Studied	PFS/OS
Lahuerta, 2010 [38]	BuMel versus Mel 200	Median PFS 41 mo versus 31 mo; median OS 77 versus 70 mo (P = .40)
Fenk, 2005 [39]	Idarubicin/Mel/Cy versus Mel 100 mg/m^2 × 2; IFN maintenance for all patients	No difference in EFS and OS TRM 20% versus 0% in Mel 200 arm
Vela-Ojeda, 2007 [40]	BCNU/etoposide/Mel versus Mel 200	Median OS 36 mo versus 86 mo (P = .08)
Palumbo, 2010 [41]	Mel 200 mg/m^2 × 2 versus Mel 100 mg/m^2 × 2	Median PFS 31.4 versus 26.2 mo (P = .01); 5-yr OS 61.8 versus 47.7% (P = .13)

Prospective, randomized studies using Consolidation after Auto-HCT

Author	Study Details	Response Data	PFS Data	OS Data
Mellqvist, 2013 [77]	Bortezomib × 20 doses versus no consolidation	Upgrade from PR favoring consolidation arm (P = .007)	Favoring consolidation arm (P = .05)	No difference
Spencer, 2009 [78]	Thal-pred versus prednisone	CR + VGPR rate favoring Thal-pred arm (P < .001)	Favoring Thal-pred arm (P < .001)	Favoring Thal-pred arm (P = .004)
Cavo, 2012 [79]	VTD versus TD consolidation; dex maintenance for all	CR/nCR rate favoring VTD arm (P = .02)	Favoring VTD arm (P = .042)	No difference

Prospective studies using novel agents for Maintenance therapy after Auto-HCT

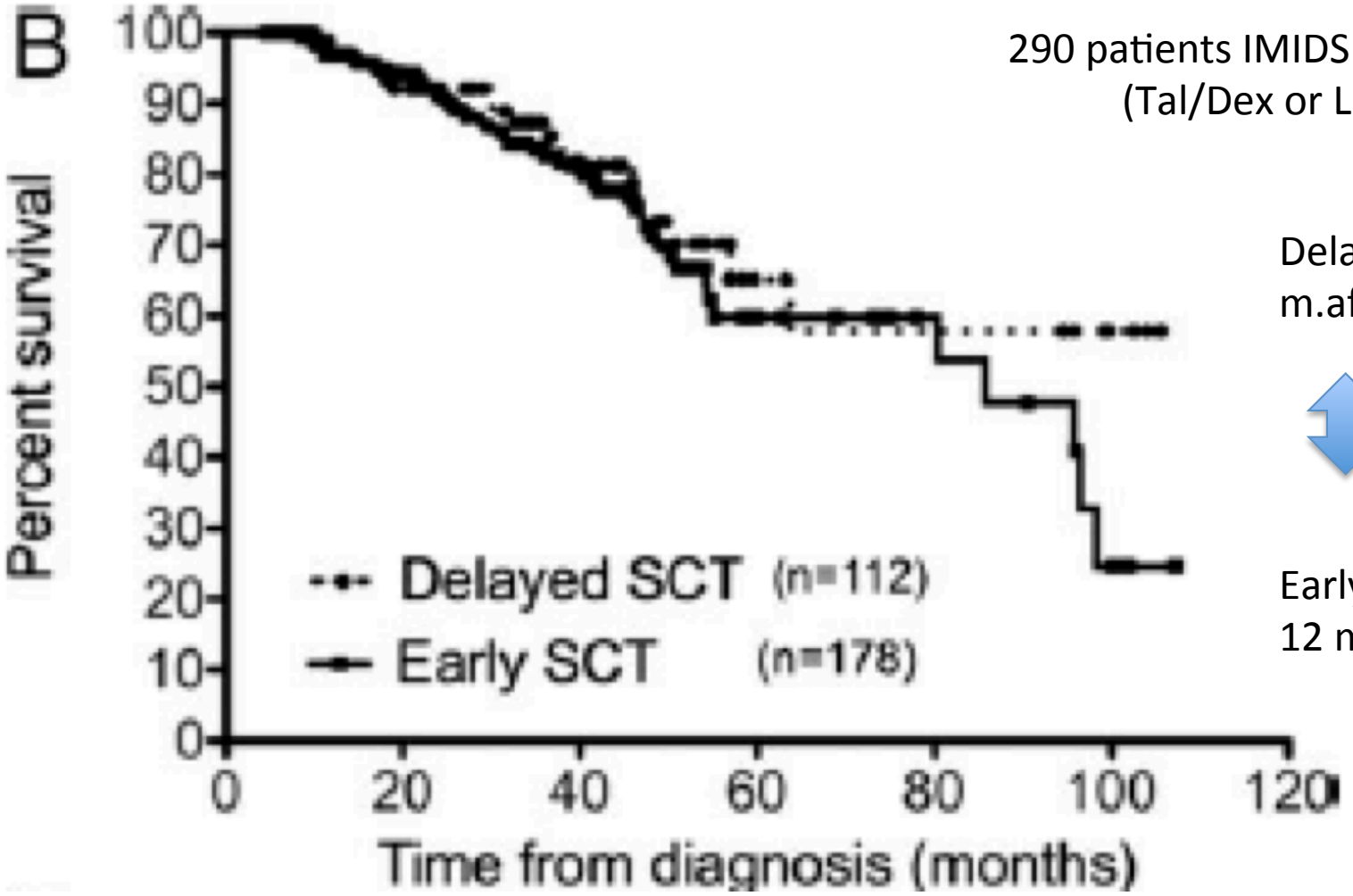
Author	Study Details	Response Data	PFS Data	OS Data
Attal, 2006 [84]	No maintenance versus pamidronate versus Thal-pamidronate	CR favoring Thal-pamidronate ($P = .03$)	EFS favoring Thal-pamidronate ($P < .009$)	Favoring Thal-pamidronate ($P < .04$)
Maiolino, 2012 [85]	Dex versus Thal-dex	No difference	Favoring Thal-dex ($P = .002$)	No difference
Stewart, 2013 [86]	No maintenance versus Thal-pred	Not reported	Favoring Thal-pred ($P < .0001$)	No difference
Morgan, 2012 [87]	No maintenance versus Thal		Favoring Thal ($P < .001$)	No difference
McCarthy, 2012 [88]	Len versus placebo	Not reported	Favoring Len ($P < .001$)	Favoring Len ($P = .03$)
Attal, 2012 [89]	Consolidation Len→Len maintenance versus placebo	CR/VGPR rates favoring Len maintenance ($P = .009$)	Favoring Len maintenance ($P < .001$)	No difference
Palumbo, 2014 [11]	MPR × 6 and Mel 200 auto-HCT × 2 arms both randomized to ± Len maintenance	Not reported for non-maintenance arms	For auto-HCT group PFS favored maintenance arm: 64.7 versus 37.4 mo	No difference due to maintenance for auto-HCT group



Multiple Myeloma ESMO Cinical Pratice Guidelines for diagnosis, treatment and follow-up.

Moreau P et al. Annals of Oncology 2017; 0:1-11

Early Versus Delayed Autologous Transplantation After Immunomodulatory Agents-Based Induction Therapy in Patients With Newly Diagnosed Multiple Myeloma



290 patients IMIDS initial therapy
(Tal/Dex or Len/Dex)

Delayed ASCT:>12
m.after diagnosis

No difference

Early ASCT:within
12 m. of diagnosis

Kumar SK et al. Cancer 2011;

Questions

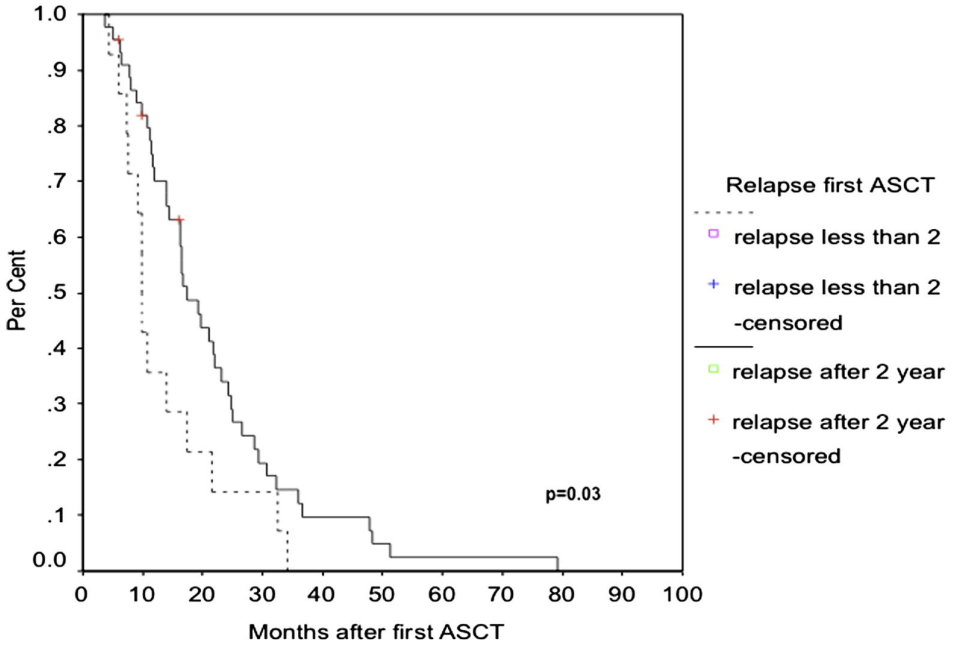
ASCT: transplant or not transplant

Single vs tandem ASCT

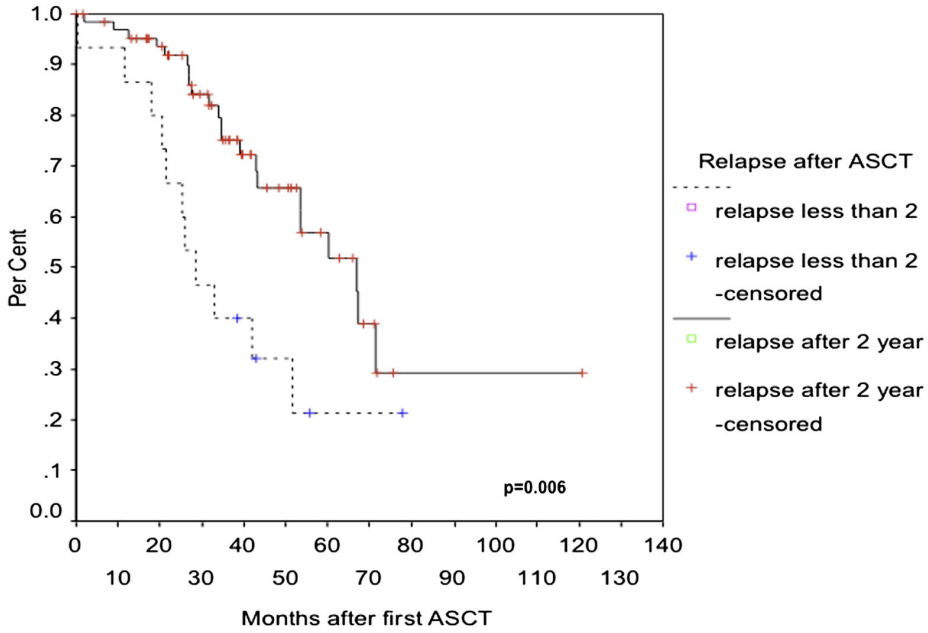
Second ASCT as salvage therapy?

Second Autologous Stem Cell Transplantation as Salvage Therapy for Multiple Myeloma: Impact on Progression-Free and Overall Survival

Progression-free survival for MM patients undergoing a second ASCT as salvage therapy according to the length of remission from the first ASCT.

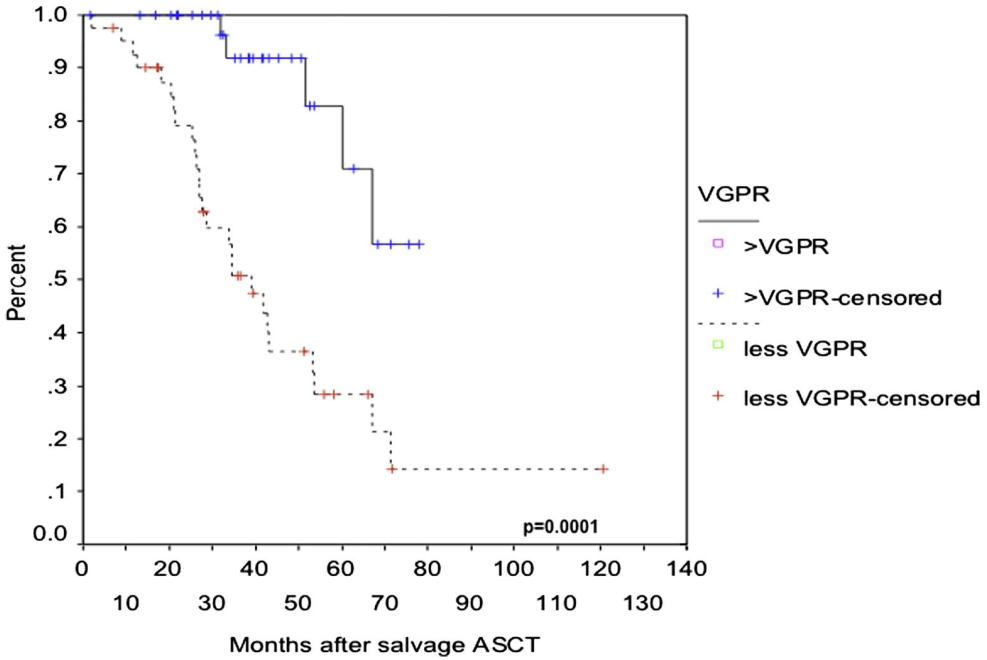


Overall survival for MM patients undergoing a second ASCT as salvage therapy according to the length of remission from the first ASCT.

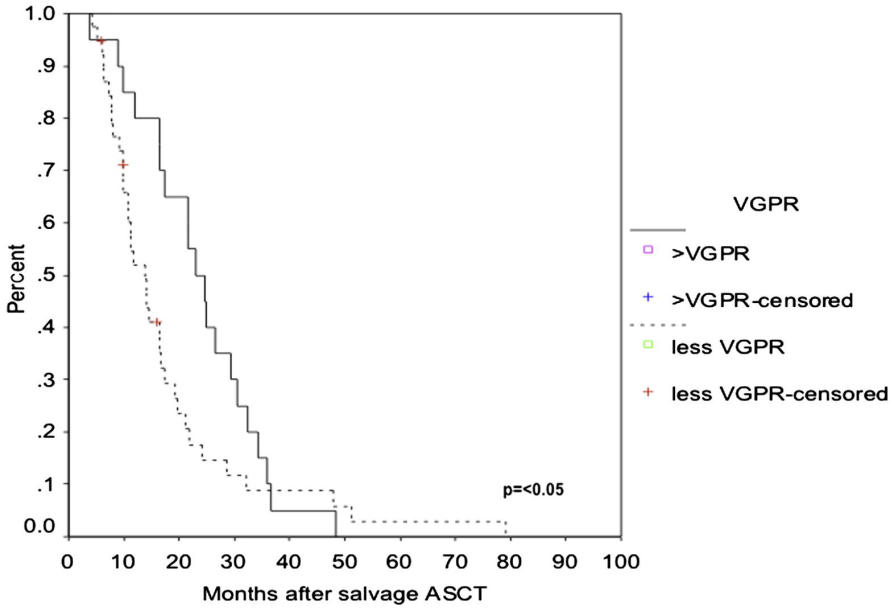


Jmenez-Zepeda VH et al. Biol Blood Marrow Transplant 2012: I 8: 773-9

Overall survival for MM patients undergoing a second ASCT as salvage therapy according to the achievement of at least very good partial response.

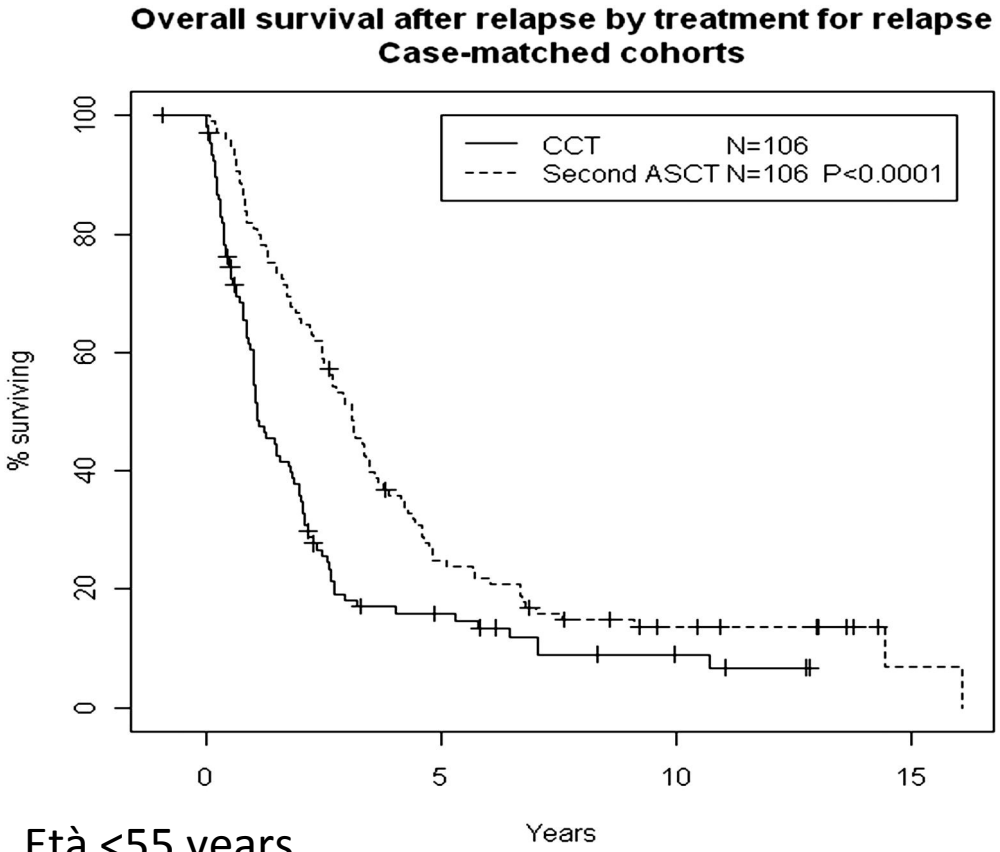


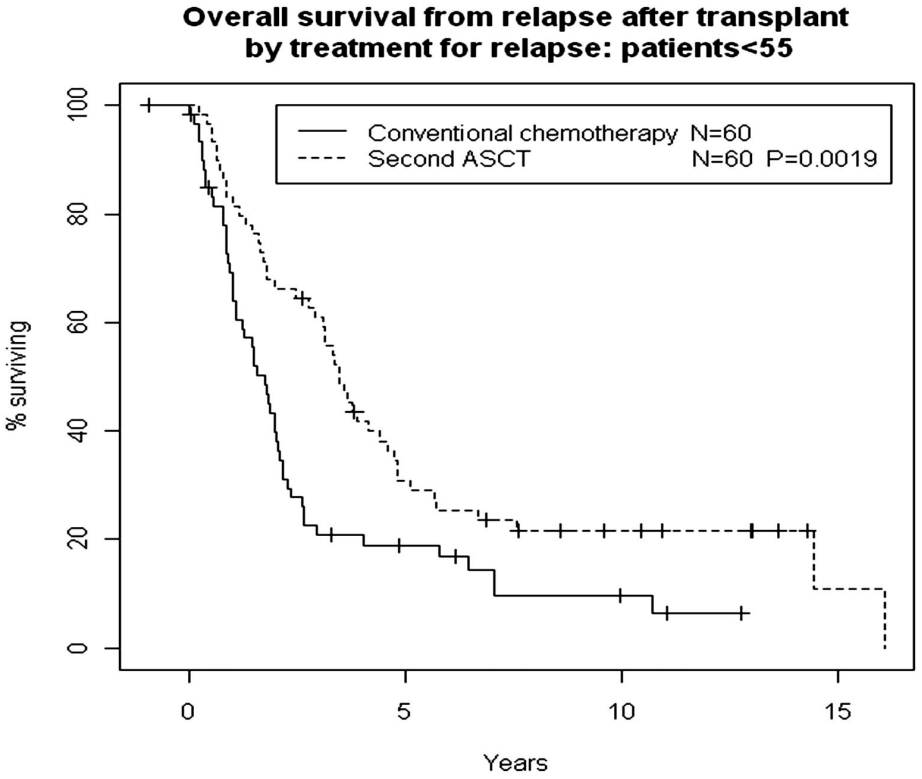
Progression-free survival for MM patients undergoing a second ASCT as salvage therapy according to the achievement of at least very good partial response.



Jmenez-Zepeda VH et al. Biol Blood Marrow Transplant 2012: I 8: 773-9

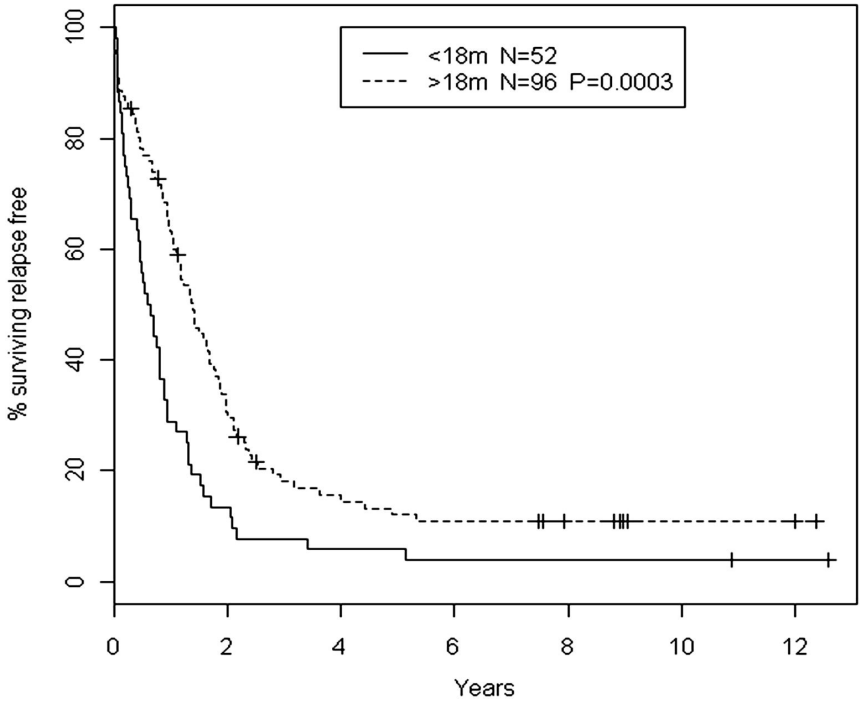
Factors Influencing the Outcome of a Second Autologous Stem Cell Transplant (ASCT) in Relapsed Multiple Myeloma: A Study from the British Society of Blood and Marrow Transplantation Registry

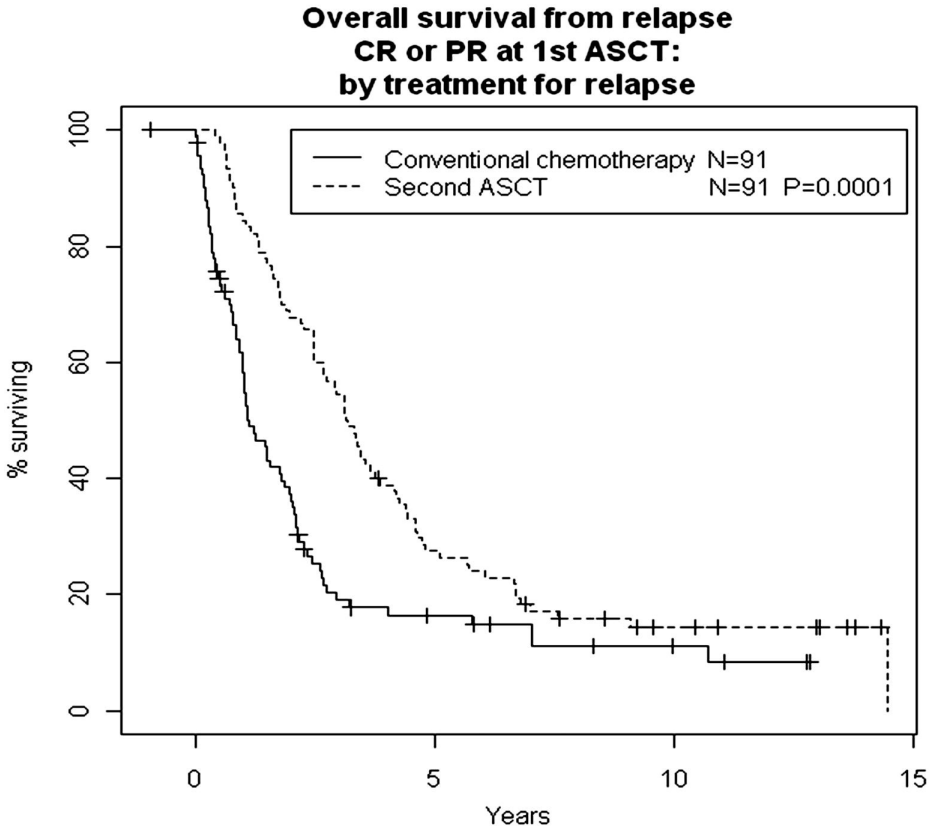




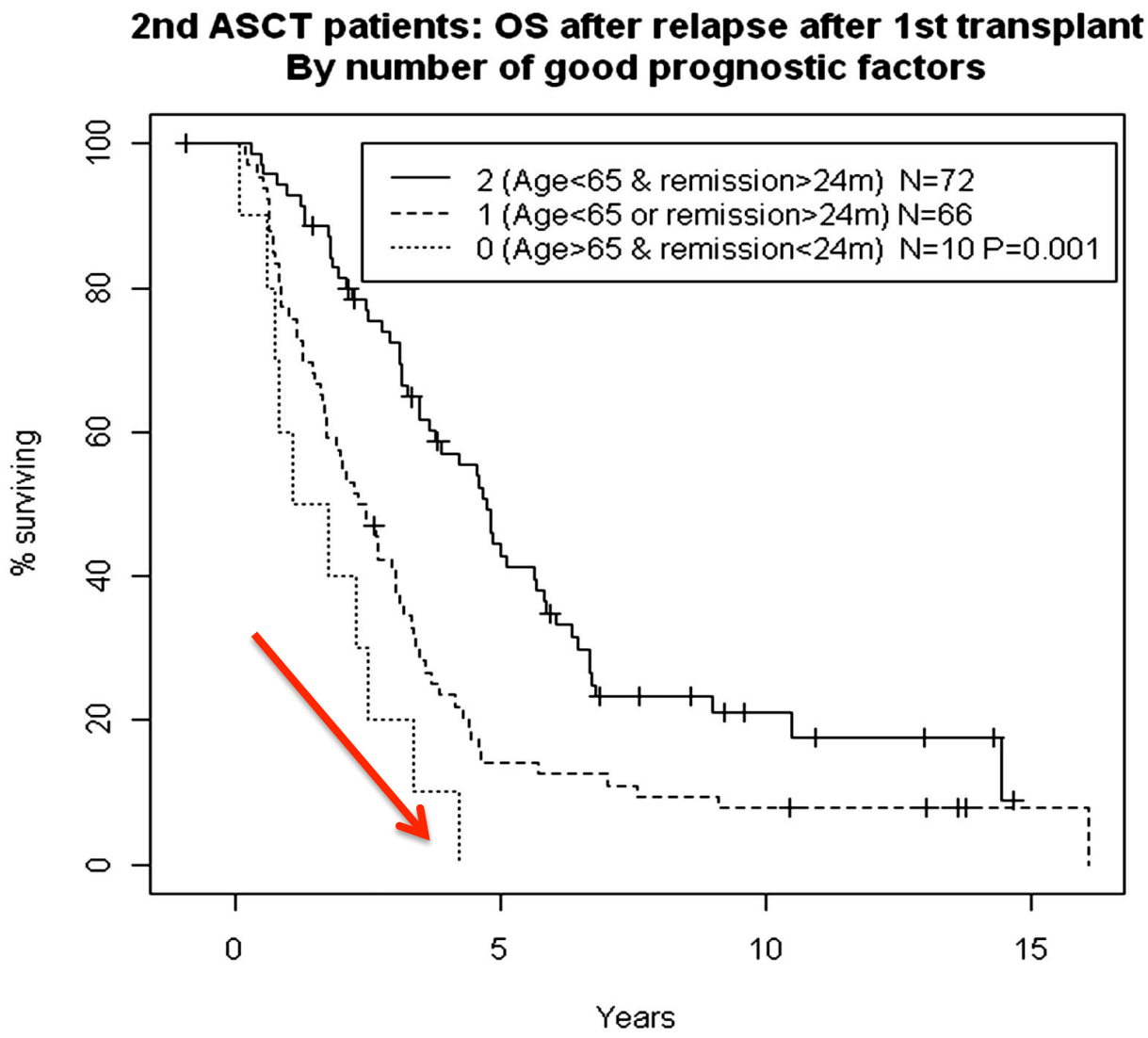
Età <55 years
β2MG<2,5
Remission lenght >9 m. from 1°
ASCT

Cook G et al BiolBlood Marrow Transplant 2011; 17: 1638-45





Cook G et al BiolBlood Marrow Transplant 2011; 17: 1638-45



Cook G et al BiolBlood Marrow Transplant 2011; 17: 1638-45

Questions

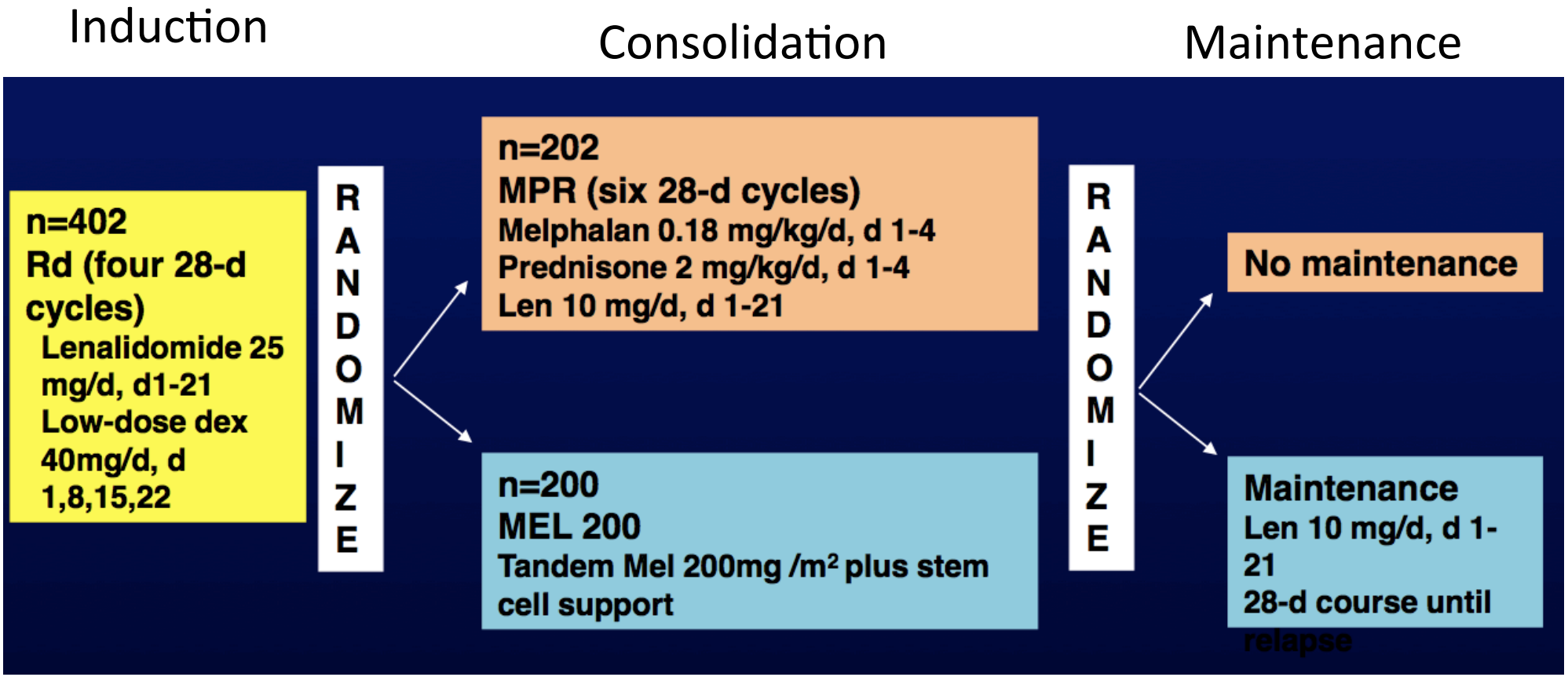
ASCT: transplant or not transplant

Single vs tandem ASCT

Second ASCT as salvage therapy?

Autologous Transplantation and Maintenance Therapy in Multiple Myeloma

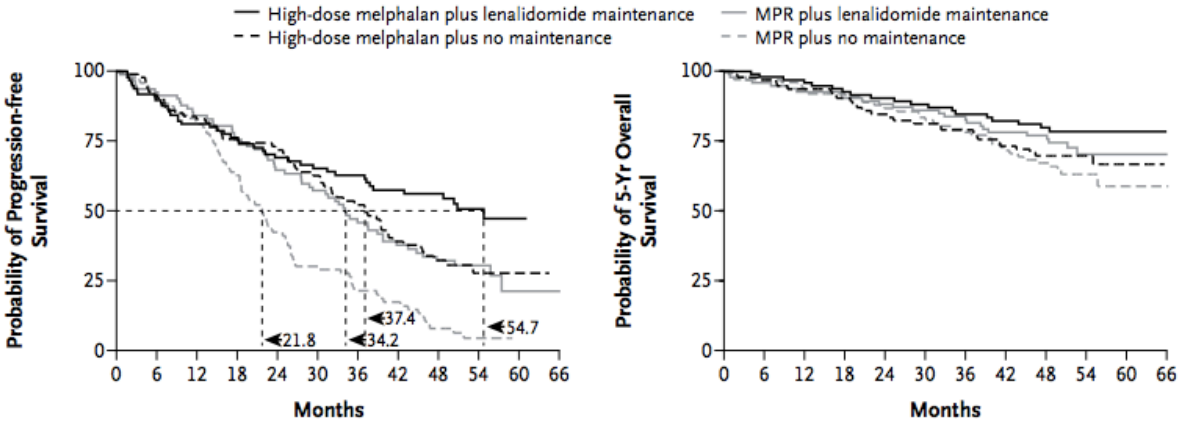
Phase 3: MPR vs Tandem ASCT



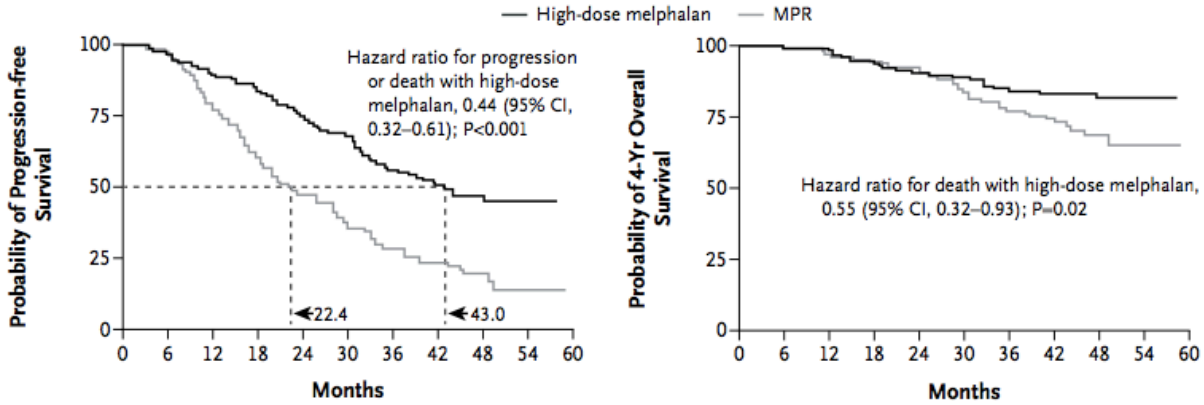
Primary end point: PFS

Palumbo A et al. N Engl J Med 2014; 37 (10): 895-905

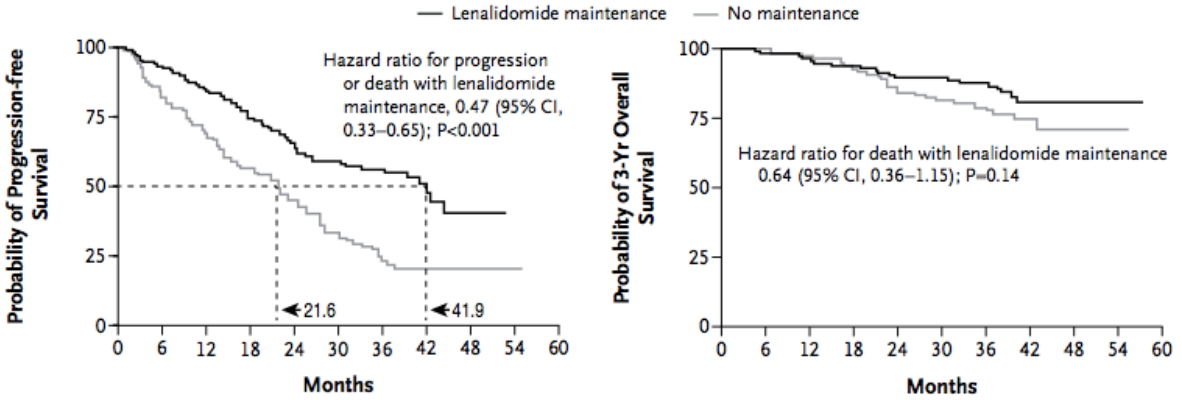
A From Time of Diagnosis



B From Start of Consolidation



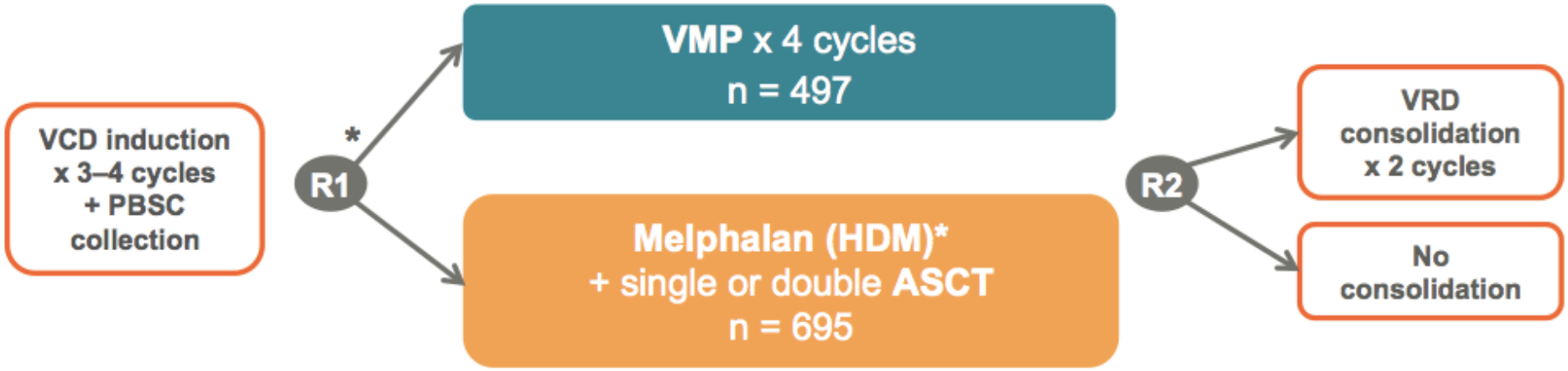
C From Start of Maintenance



CONCLUSION

- ASCT remains the more effective therapeutic option in NDMM patients
- The maimtenance therapy with lenalidomide, as compared with no maintenance, significantly reduces the risk of disease progression

ASCT vs VMP
EMN02/HO95 MM phase 3 trial



All patients received lenalidomide maintenance until relapse/progression

* **Randomization was to VMP vs HDM-1 (1:1) in centres with a single ASCT policy and to VMP vs HDM-1 vs HDM-1-2 (1:1:1) in centres with a double ASCT policy**

Stratification: ISS I vs II vs III

Primary endpoint: PFS from R1 (VMP vs ASCT)

Cavo M, et al. Presented at ASH 2016. Blood. 2016;128:abstract 673.
Cavo M, et al. Presented at ASCO 2016. J Clin Oncol. 2016;34 Suppl:abstract 8000.

Cavo M et al. Blood 2016; 128: Abst. 673 ASH
Cavo M et al. J cl Oncol 2016; Abst.8000 ASCO

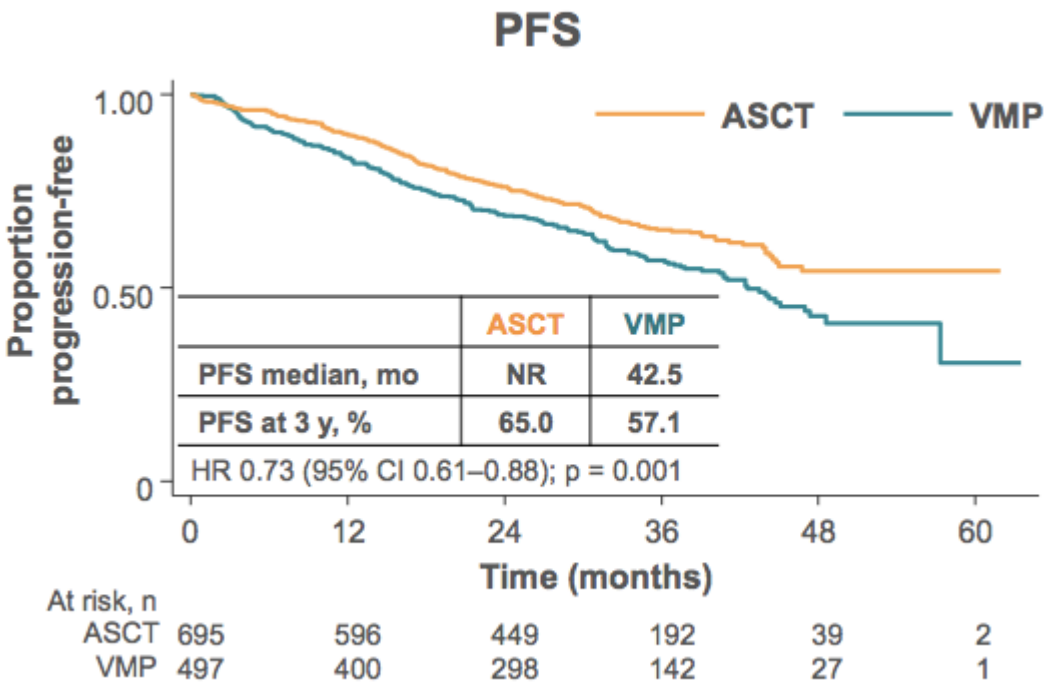
ASCT vs VMP: best response and PFS
EMN02/HO95 MM phase 3 trial

EMN02/HO95 MM trial

Best response

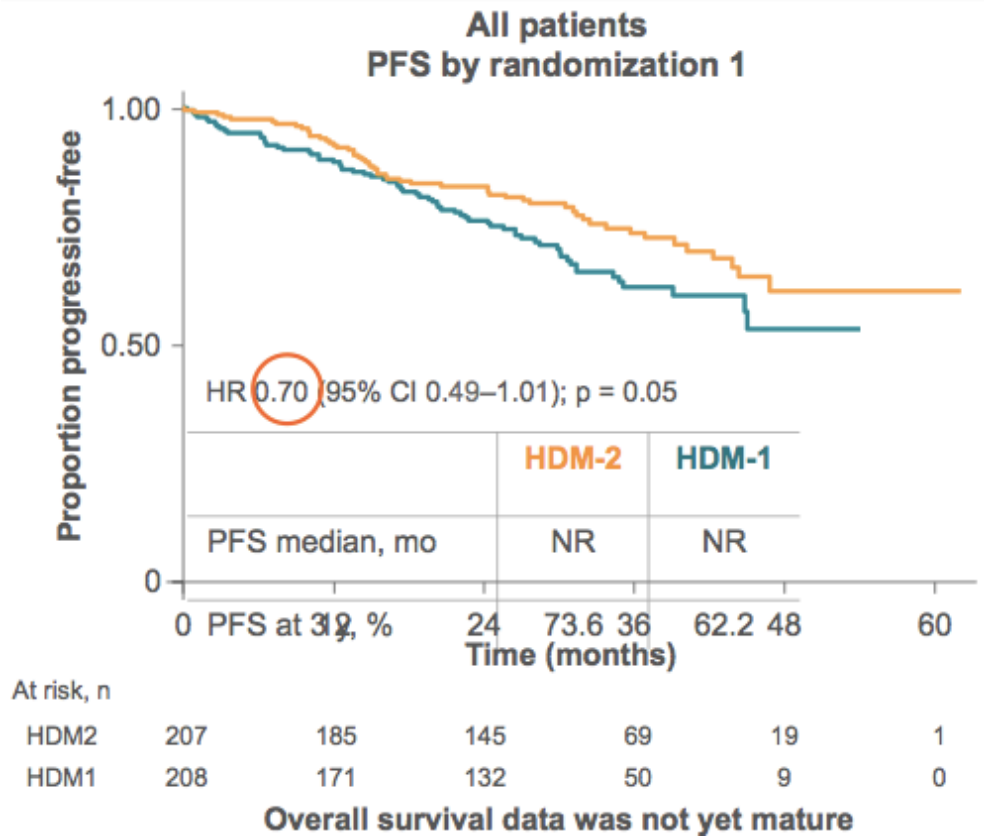
	ASCT (N = 695)	VMP (N = 497)	p value
sCR, %	17.0	18.2	
CR, %	25.3	25.3	
VGPR, %	43.2	30.4	
PR, %	11.2	14.9	
< PR, %	3.3	11.3	
≥ VGPR, %	85.5	73.8	< 0.0001

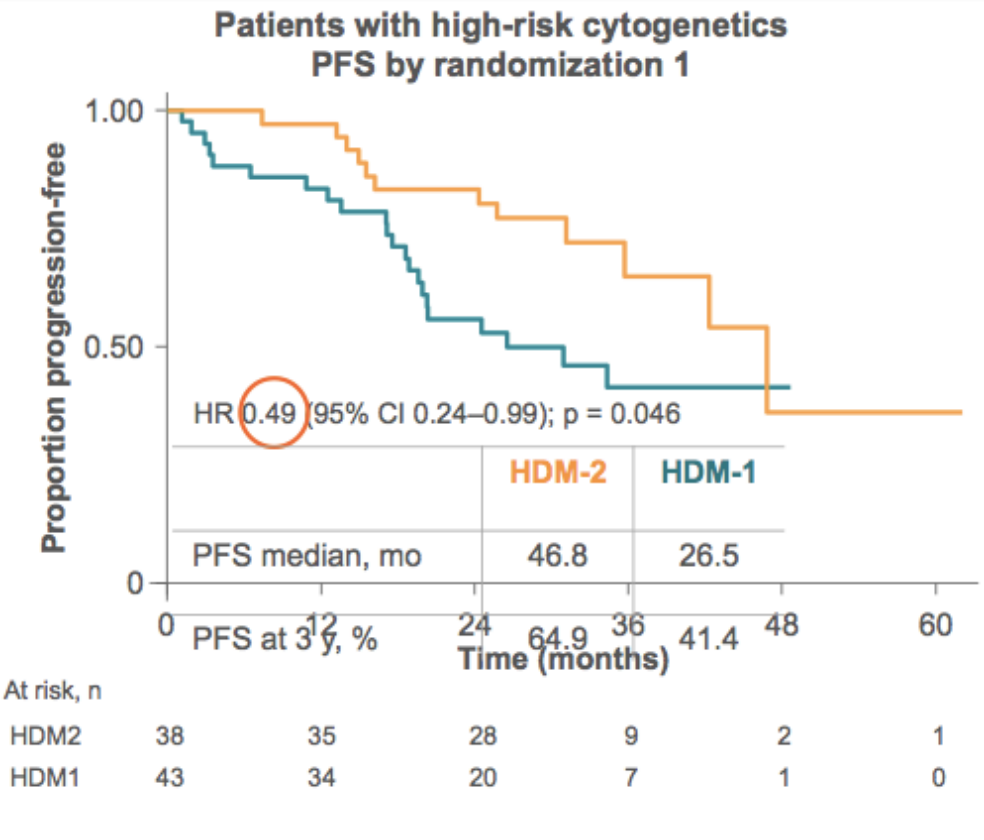
- Improved PFS in patients with high-risk cytogenetics who received ASCT; HR 0.53 (95% CI 0.37–0.76); p = 0.001



Cavo M et al. Blood 2016; 128: Abst. 673 ASH
Cavo M et al. J cl Oncol 2016; Abst.8000 ASCO

Up front single vs double ASCT EMN02/HO95 MM phase 3 trial



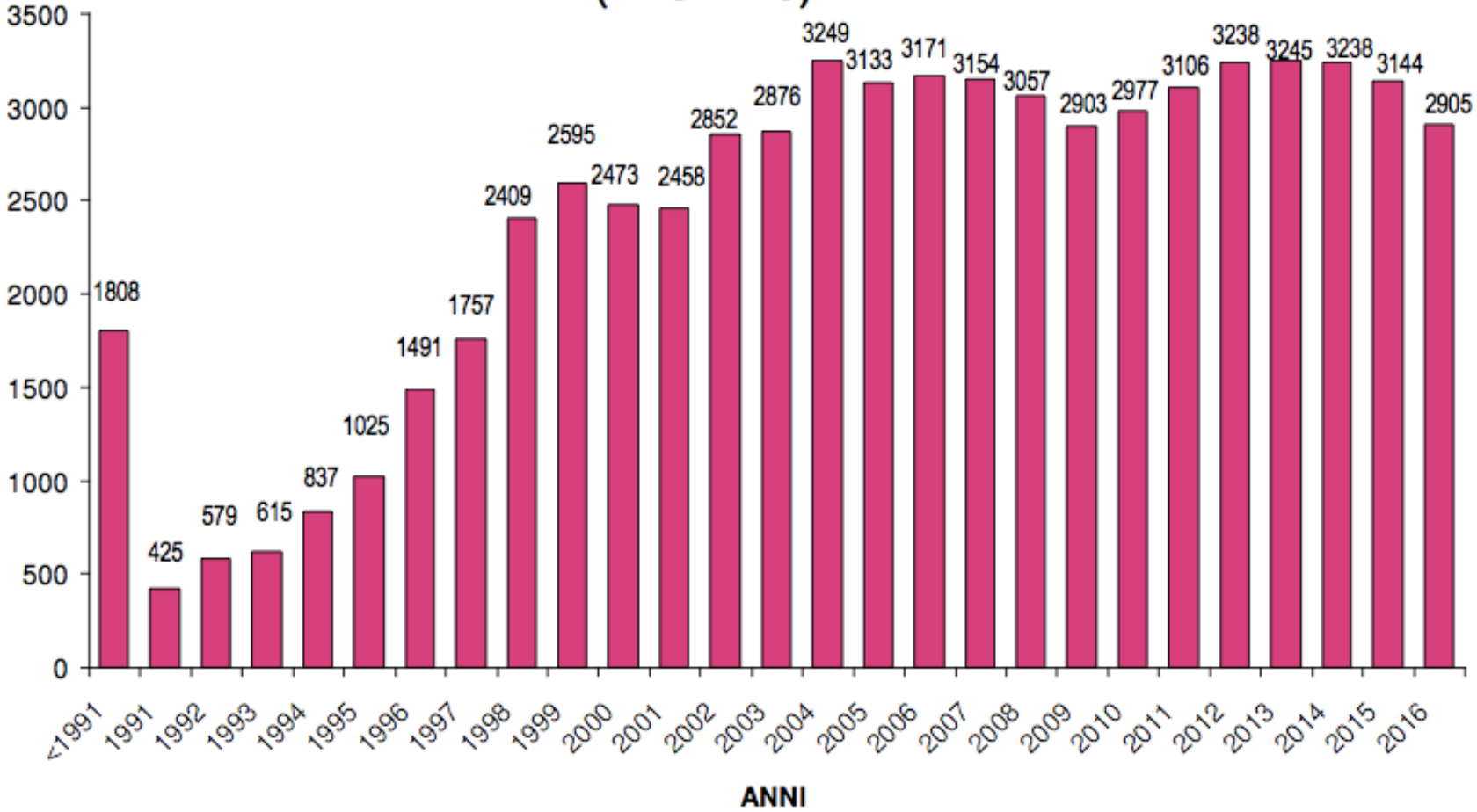


Cavo M et al. Blood 2016; 128: Abst. 673 ASH
Cavo M et al. J cl Oncol 2016; Abst.8000 ASCO

GITMO Trapianto Autologo

Autotrapianti registrati

(n=64720)



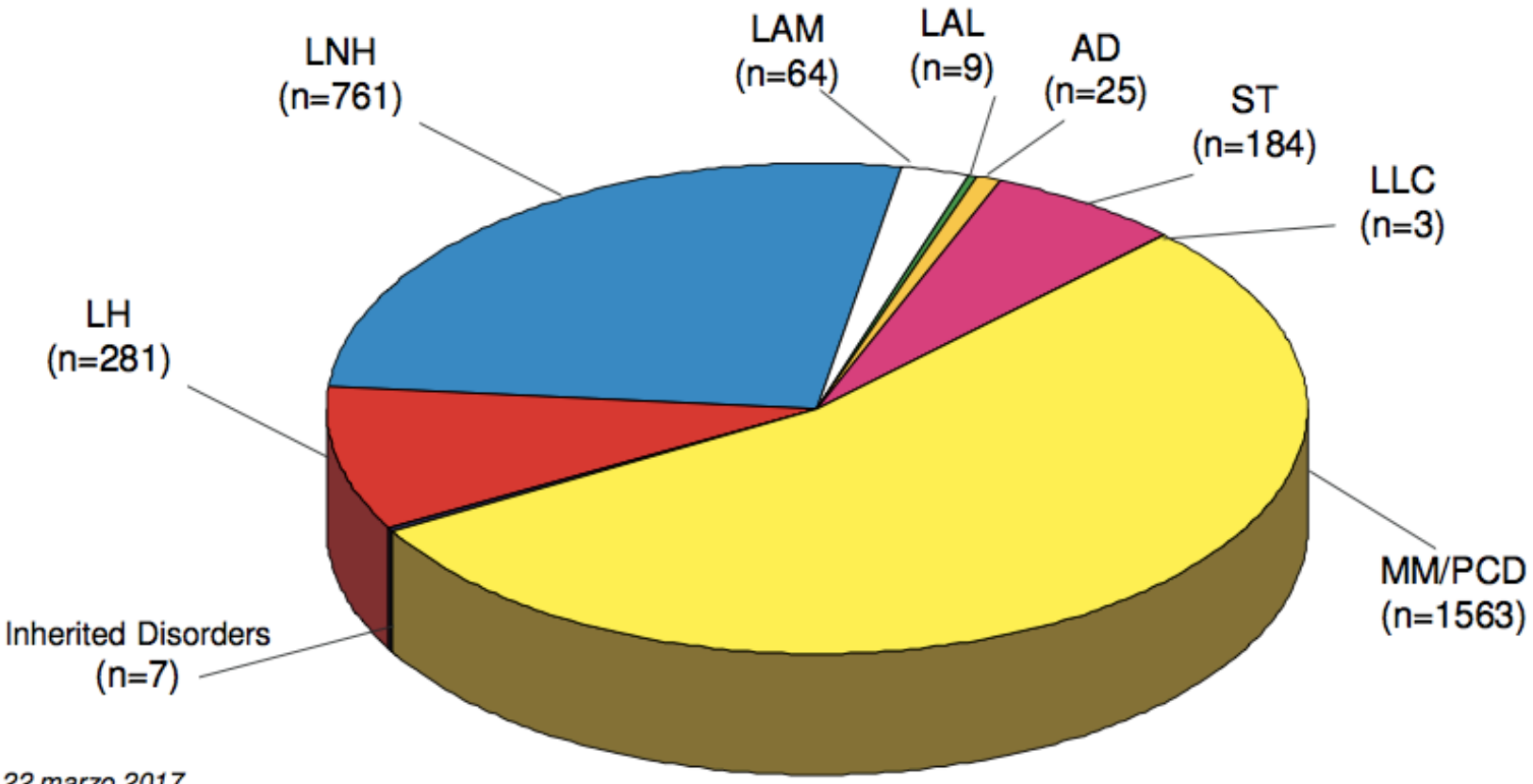
al 22 marzo 2017

GITMO

GITMO Trapianto Autologo

Numero Trapianti per principali patologie

Attività 2016



al 22 marzo 2017

GITMO

Rete Ematologica Pugliese

Ematologia AOU – OO RR Foggia
Gaetano Palumbo
Silvana F. Capalbo

Ematologia AOU Policlinico Bari
Paola Curci/Rita Rizzi
Giorgina Specchia

Ematologia ASL Lecce
Giovanni Reddiconto
Nicola Di Renzo

Ematologia IRCCS San Giovanni Rotondo
Antonietta Falcone
Nicola Cascavilla

Ematologia IRCCS Bari
Carla Minoia
Attilio Guarini

Ematologia ASL Taranto
Giulia Palazzo
Patrizio Mazza

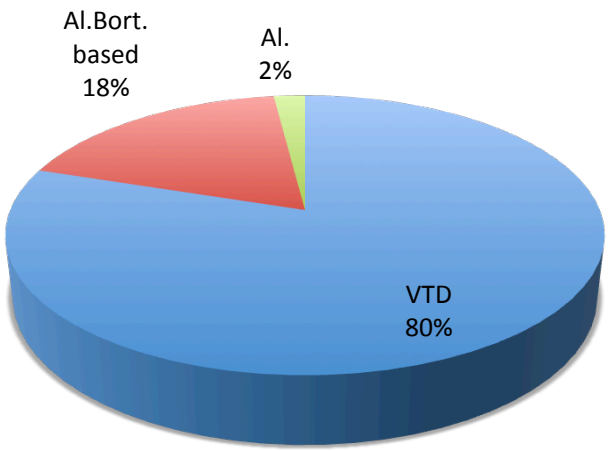
Ematologia ASL Barletta
Lucia Ciuffreda
Pino Tarantini

Ematologia ASL Brindisi
Giuseppe Mele
Domenico Pastore

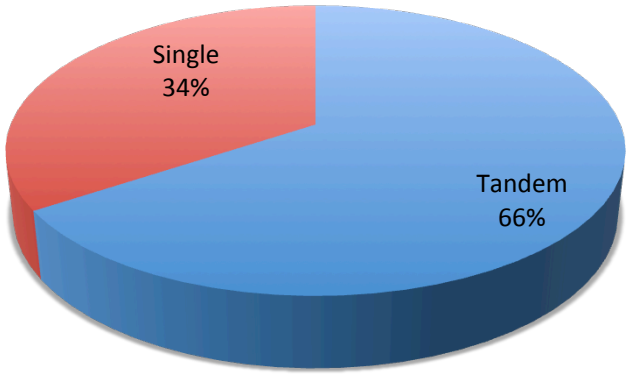
Ematologia Tricase
Mariangela Mele
Enzo Pavone

Real-life retrospective study on the upfront treatment strategy for NDMM patients

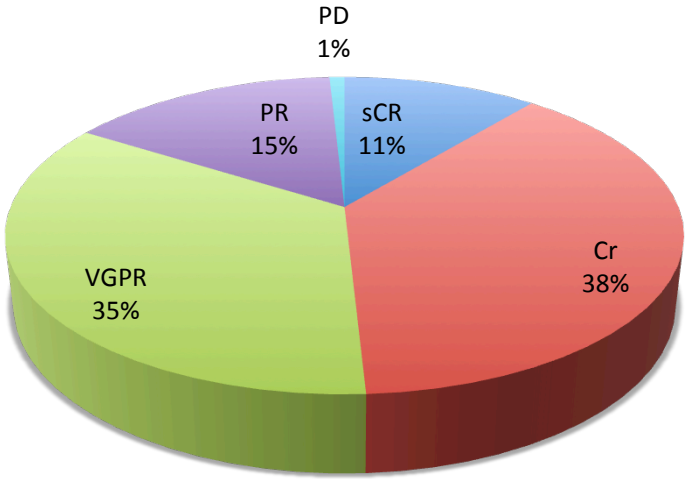
Induction treatment



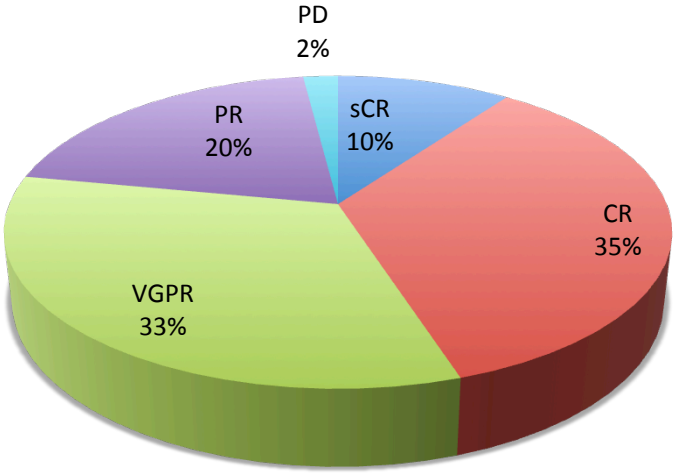
Single vs Tandem ASCT



Response post 1st ASCT



Response post 2nd ASCT



Answers

Transplant or not transplant	YES ASCT……in the future…?.
Single vs tandem ASCT	Tandem better
Second ASCT as salvage therapy?	May be…… unclear role..

BARI 2016 ; Ponte Adriatico: dalla terra al mare.