

The logo for the Società Italiana di Ematologia (SIE) features the letters 'SIE' in a stylized, red, serif font.

Società Italiana di Ematologia

A purple rectangular box containing the text 'Convegno Interregionale SIE' in a large, white, sans-serif font, with 'Delegazione Triveneto' in a smaller font below it.A scenic photograph of a mountain range with snow-capped peaks under a clear blue sky. In the foreground, there are dark green leaves and branches of a tree, partially obscuring the view.

NUOVE TERAPIE NEI LINFOMI B AGGRESSIVI E NEL MIELOMA MULTIPLO

Il ruolo del trapianto autologo nell'era dei nuovi farmaci



Dr. Gregorio Barilà, MD, PhD
U.O.C. Ematologia, Ospedale san Bortolo, Vicenza



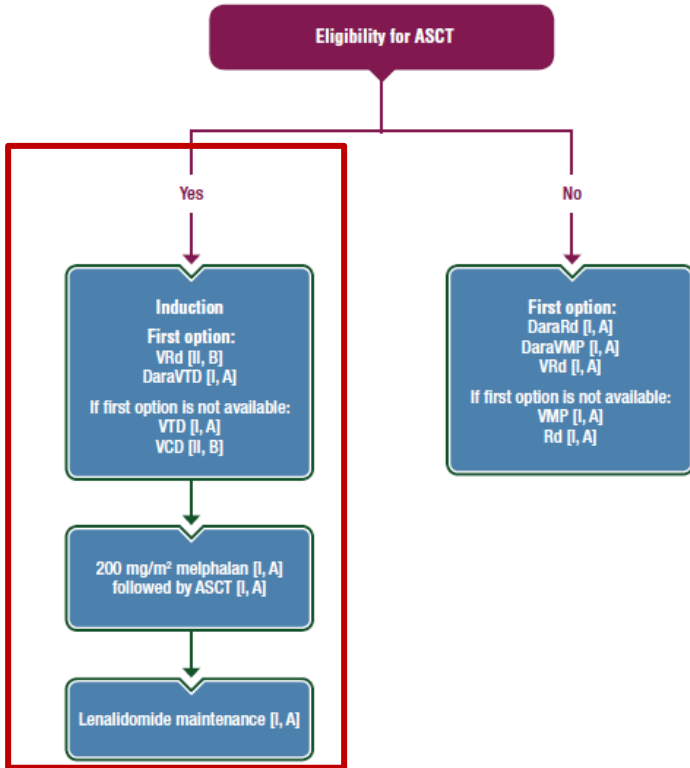
CRO Aviano (PN) - 9 ottobre 2024

Convegno Regionale SIE



Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Janssen			X			X	
Amgen			X				
Takeda							
BMS						X	
Sanofi							
GSK							
Menarini						X	
Pfizer						X	

ESMO 2021



RV-MM-EMN441/RV-MM-PI-209

**CDR/MPR
Vs
HDM-ASCT**

IFM2009/DETERMINATION

**VRD
Vs
HDM-ASCT**

EMN02-HO95

**VMP
Vs
HDM-ASCT**

FORTE

**KRD
Vs
HDM-ASCT**

N=529

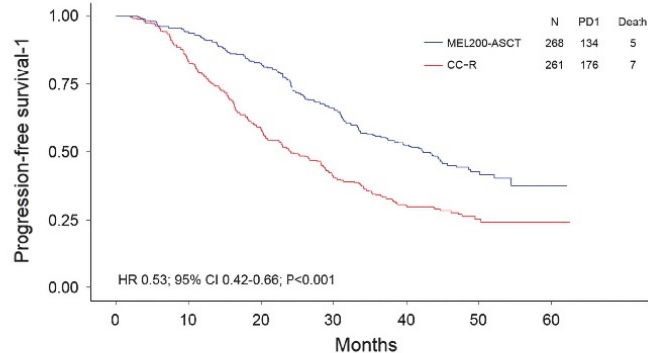
RV-MM- EMN-441/RV-MM-PI-209

HDM-ASCT vs R+chemo



PFS

42 vs 24 months

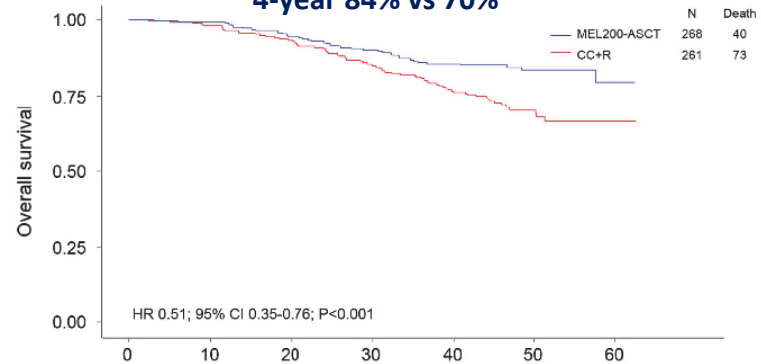


	0	10	20	30	40	50	60
MEL200-ASCT	268	239	205	160	127	45	3
CC+R	261	211	145	99	72	23	4

Numbers at risk

OS

4-year 84% vs 70%



	0	10	20	30	40	50	60
MEL200-ASCT	268	255	236	220	205	82	6
CC+R	261	249	235	209	182	66	5

Numbers at risk

Gay F. et al Leukemia, 2017

Convegno Regionale SIE



N=1503

EMN02/HO95

HDM-ASCT vs Bortezomib+chemo

VCD

R

HDM-ASCT x1-2

R

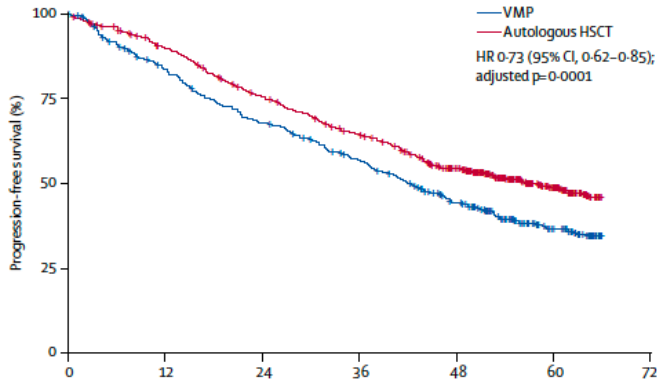
VRD

R maintenance

VMP

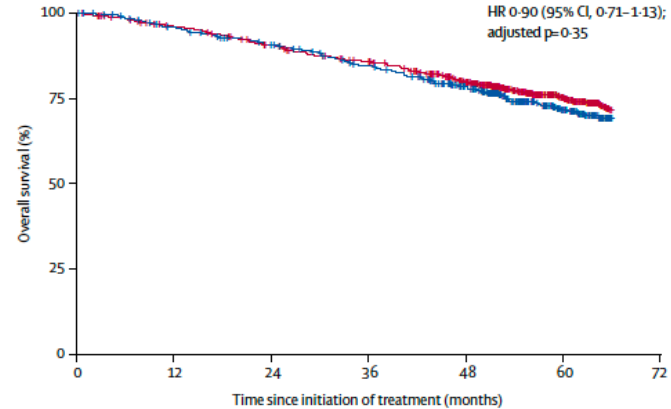
R maintenance

PFS
57 vs 42 months



Number at risk (number censored)	0	12	24	36	48	60	72
Autologous HSCT	702 (0)	616 (17)	509 (24)	428 (31)	334 (59)	178 (188)	..
VMP	495(0)	401 (13)	324 (14)	266 (21)	189 (39)	97 (104)	..

OS
5 year 75.1% vs 71.6%



Number at risk (number censored)	0	12	24	36	48	60	72
Autologous HSCT	702 (0)	658 (16)	614 (24)	569 (36)	487 (78)	276 (268)	..
VMP	495 (0)	463 (12)	430 (20)	391 (31)	331 (62)	174 (198)	..

.. Cavo M. et al Lancet Haematol, 2020

IFM2009/DETERMINATION

HDM-ASCT vs VRD

R

VRD x 3

HDM-ASCT

VRD x 2

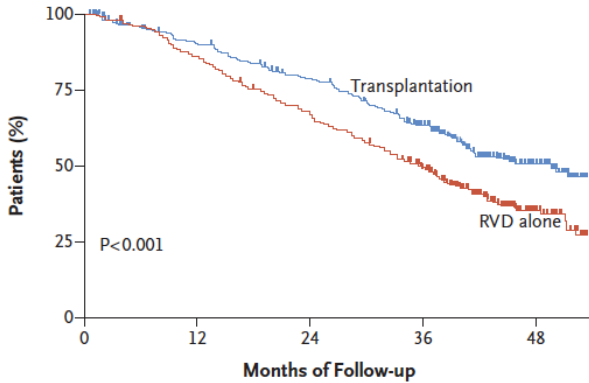
R maintenance *

VRD x 3

VRD x 5

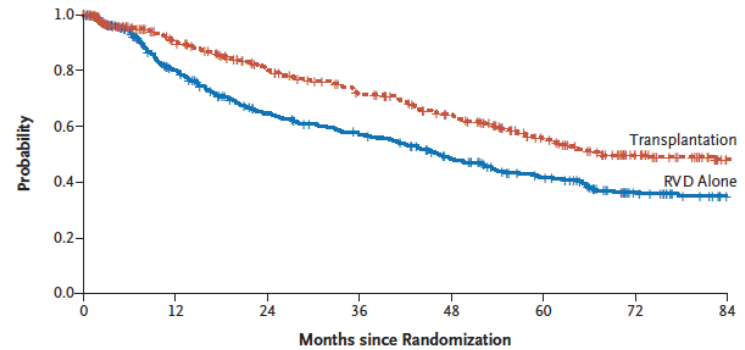
*IFM 2009: 1 year maintenance
Determination: until progression maintenance

IFM 2009 (n=700)
PFS 47 vs 35 months



No. at Risk		0	12	24	36	48
RVD alone	350	294	228	157	32	
Transplantation	350	308	264	196	50	

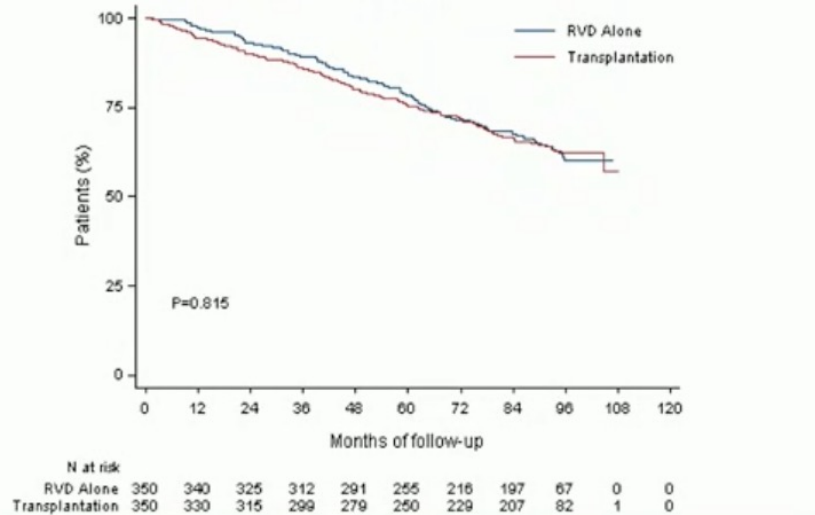
Determination (n=722)
PFS 68 vs 46 months



No. at Risk		0	12	24	36	48	60	72	84
Transplantation	365	276	226	191	160	118	77	42	
RVD Alone	357	250	187	160	126	96	60	40	

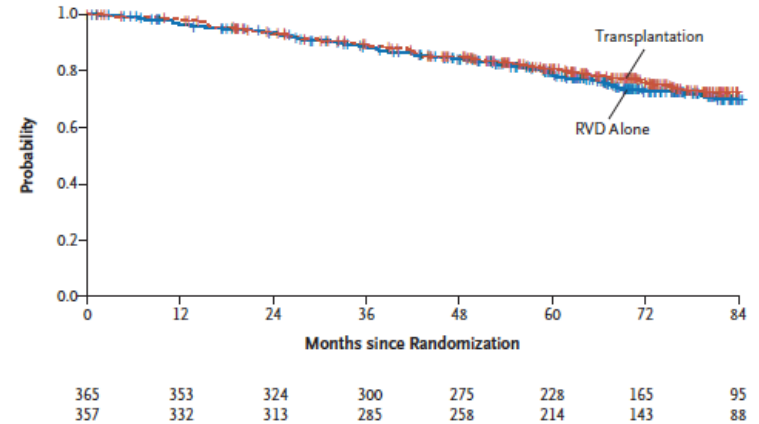
Attal M. et al, NEJM, 2017; Richardson P. et al, NEJM 2022

IFM2009



Trapianto di salvataggio=77% nel braccio VRD alone

DETERMINATION



Trapianto di salvataggio=28% nel braccio VRD alone

Perrot A. et al, ASH, 2020; Richardson P. et al, NEJM 2022

Convegno Regionale SIE



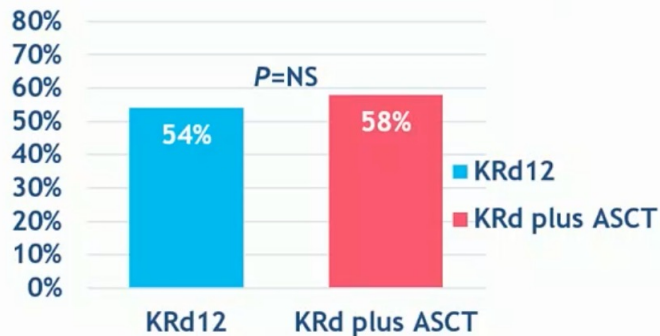
N=476

FORTE

HDM-ASCT vs KRd



Pre-maintenance MRD negativity rates



12-month sustained MRD negativity rates



Gay F. et al Lancet Oncol, 2021; Mina R. EHA, 2021

Convegno Regionale SIE



N=476

FORTE

HDM-ASCT vs KRd

R



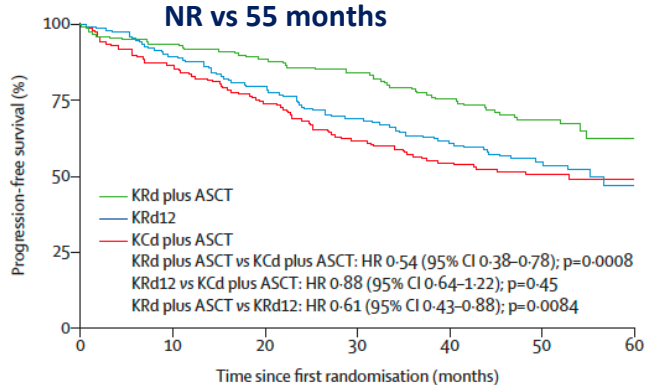
R

R maintenance

KR maintenance

PFS KRd+ ASCT vs KRd12

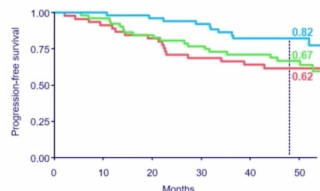
NR vs 55 months



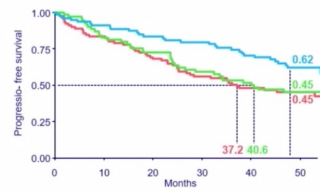
Number at risk
(number censored)

	0	10	20	30	40	50	60
KRd plus ASCT	158 (0)	147 (1)	137 (3)	129 (4)	111 (9)	61 (51)	5 (103)
KRd12	157 (0)	135 (6)	120 (6)	103 (7)	90 (9)	51 (39)	5 (81)
KCd plus ASCT	159 (0)	137 (1)	115 (3)	94 (5)	80 (8)	46 (37)	6 (76)

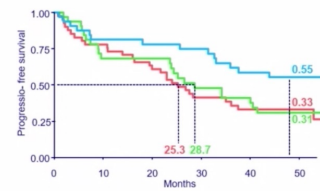
Standard risk
(N=153)



High risk
(N=243)



Double hit
(N=105)



KRd_ASCT vs. KCD_ASCT: HR 0.44, p=0.04	KRd_ASCT vs. KCD_ASCT: HR 0.57, p=0.01	KRd_ASCT vs. KCD_ASCT: HR 0.49, p=0.03
KRd_ASCT vs. KRd12: HR 0.46, p=0.04	KRd_ASCT vs. KRd12: HR 0.6, p=0.04	KRd_ASCT vs. KRd12: HR 0.53, p=0.07
KRd12 vs. KCD_ASCT: HR 0.96, p=0.9	KRd12 vs. KCD_ASCT: HR 0.95, p=0.8	KRd12 vs. KCD_ASCT: HR 0.91, p=0.75

Gay F. et al Lancet Oncol, 2021; Mina R. EHA, 2021

Singolo ASCT vs Tandem ASCT?

Convegno Regionale SIE



N=508

GIMEMA MMY-3006

R

VTD x 3

HDM-ASCT x 2

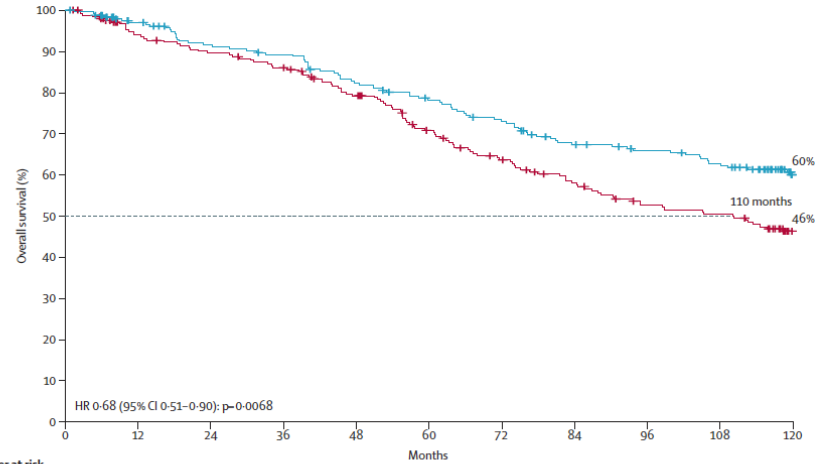
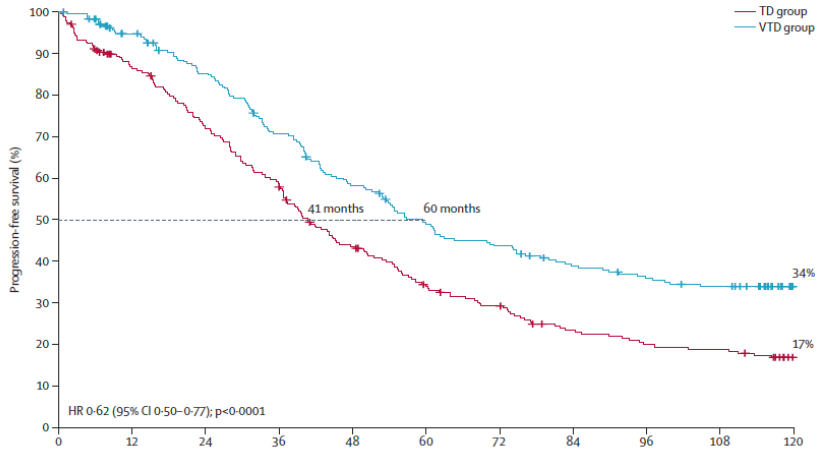
VTD x 2

Dexa maintenance

TD x 3

HDM-ASCT x 2

TD x 2



Number at risk (number censored)

Time (months)	0	12	24	36	48	60	72	84	96	108	120
TD group	238 (0)	198 (8)	165 (9)	134 (10)	97 (12)	74 (15)	62 (16)	47 (19)	40 (19)	38 (19)	26 (53)
VTD group	236 (0)	212 (12)	187 (16)	154 (17)	126 (18)	105 (20)	93 (20)	80 (23)	73 (24)	68 (25)	47 (93)

Number at risk (number censored)

Time (months)	0	12	24	36	48	60	72	84	96	108	120
TD group	238 (0)	214 (10)	203 (11)	194 (13)	174 (17)	149 (24)	131 (27)	116 (31)	102 (34)	98 (34)	74 (124)
VTD group	236 (0)	217 (12)	201 (16)	195 (17)	179 (18)	167 (21)	156 (22)	139 (26)	132 (30)	125 (31)	91 (151)

Tacchetti P. et al Lancet Haematol. 2020

Convegno Regionale SIE



N=1503

EMN02/HO95

VCD

R

HDM-ASCT x1-2

VMP

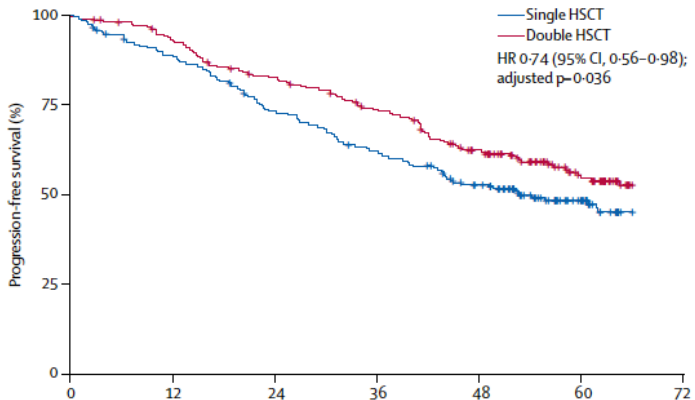
R

VRD

R maintenance

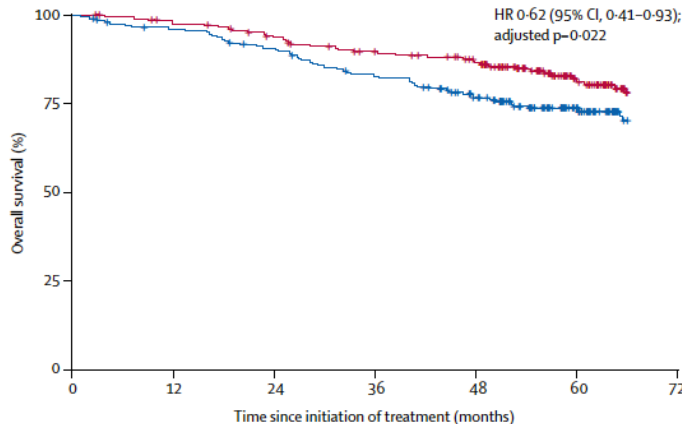
R maintenance

PFS
5 year 53.5% vs 44.9%



Number at risk (number censored)	0	12	24	36	48	60	72
Double HSCT	210 (0)	192 (4)	167 (7)	145 (11)	115 (19)	68 (54)	..
Single HSCT	209 (0)	181 (5)	147 (7)	124 (8)	97 (16)	53 (54)	..

OS
5 year 80.3% vs 72.6%



Number at risk (number censored)	0	12	24	36	48	60	72
Double HSCT	210 (0)	201 (4)	189 (8)	175 (15)	159 (24)	100 (75)	..
Single HSCT	209 (0)	195 (6)	182 (8)	164 (10)	141 (21)	85 (72)	..

Cavo M. et al Lancet Haematol, 2020

Convegno Regionale SIE



N=1503

EMN02/HO95

VCD

R

HDM-ASCT x1-2

R

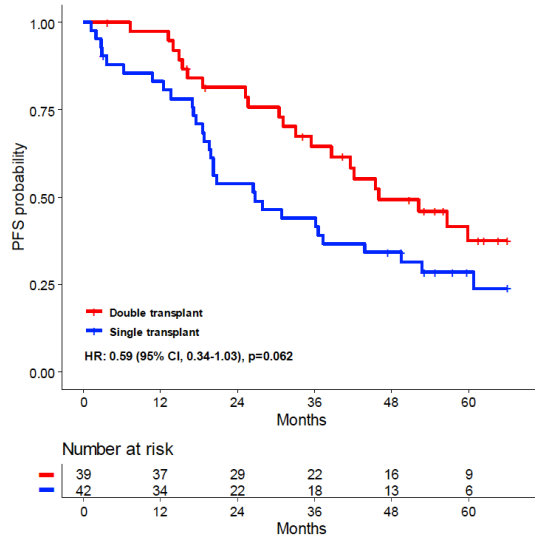
VRD

R maintenance

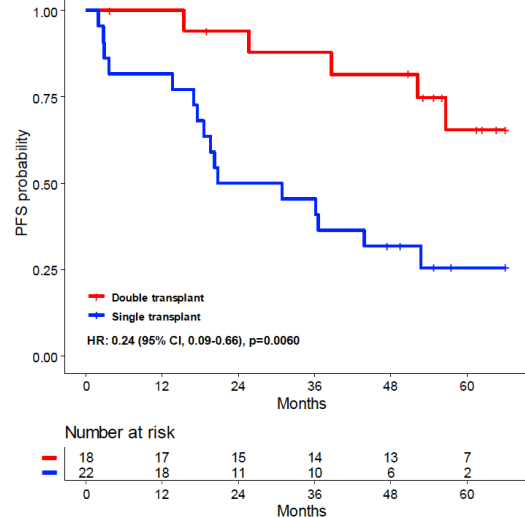
VMP

R maintenance

PFS in HR cytogenetic*



PFS in del17p



*t(4;14), t(14;16), del17p

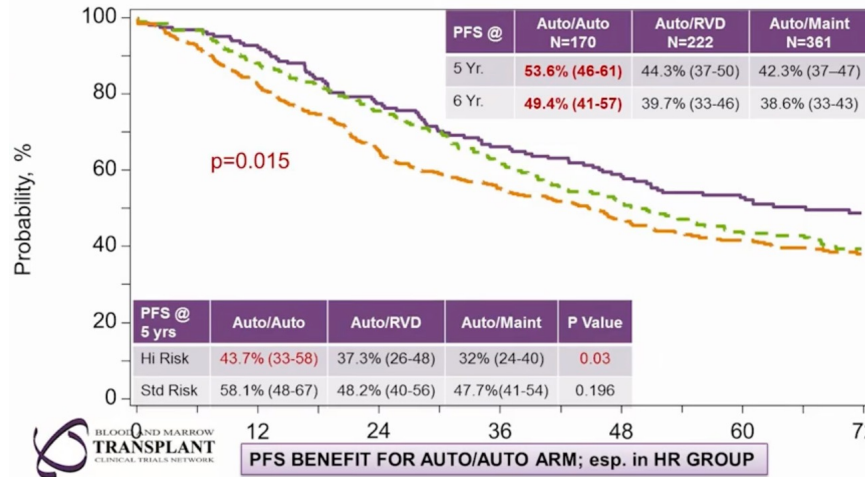
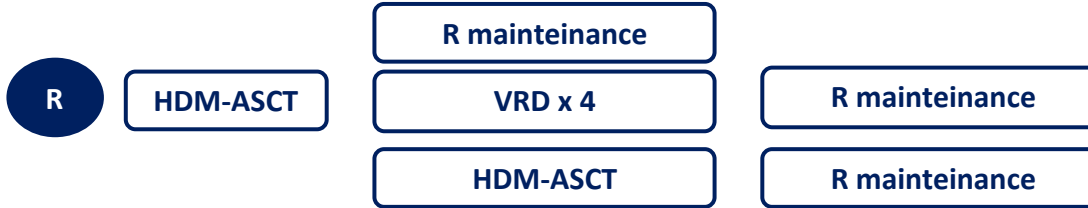
Cavo M. et al Lancet Haematol, 2020

Convegno Regionale SIE



N=758

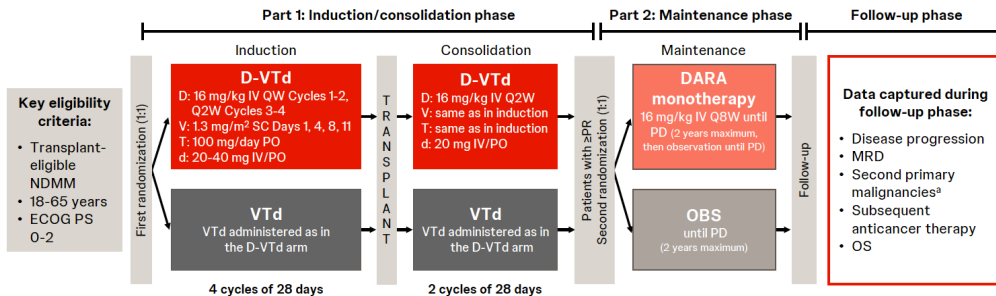
STaMINA TRIAL



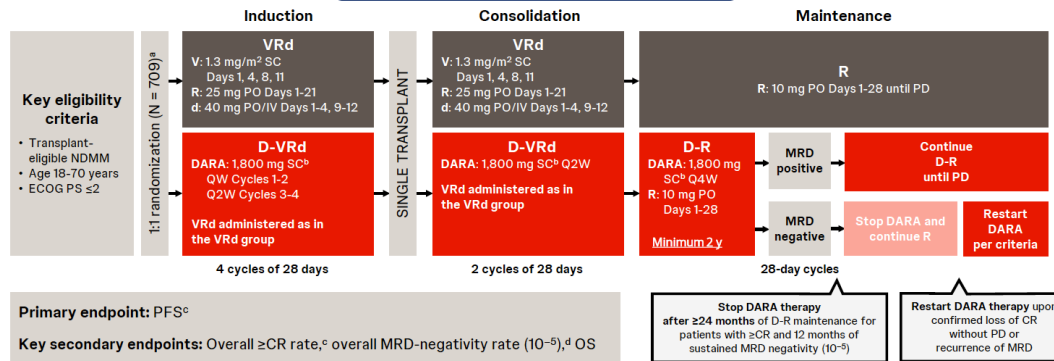
HR: *t(4;14)*, *t(14;16)*, *t(14;20)*, *del17p*, *del13p*, *aneuploidy* or $\beta 2$ *microglobulin* >5.5mg/L

Hari P. et al, ASCO, 2020

CASSIOPEIA



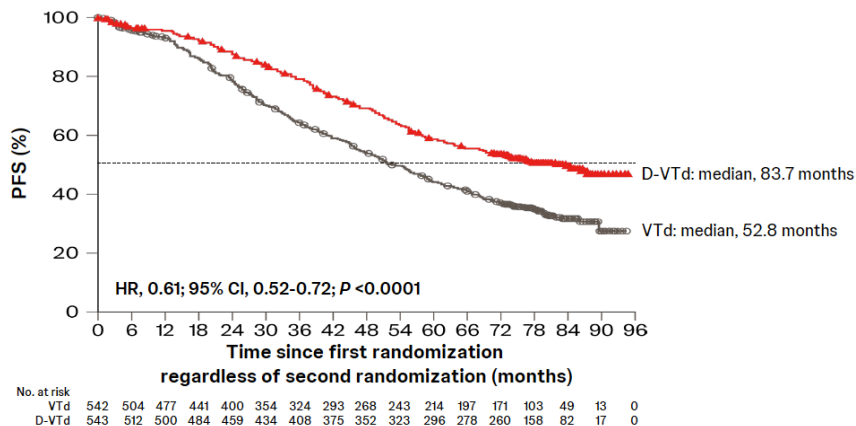
PERSEUS



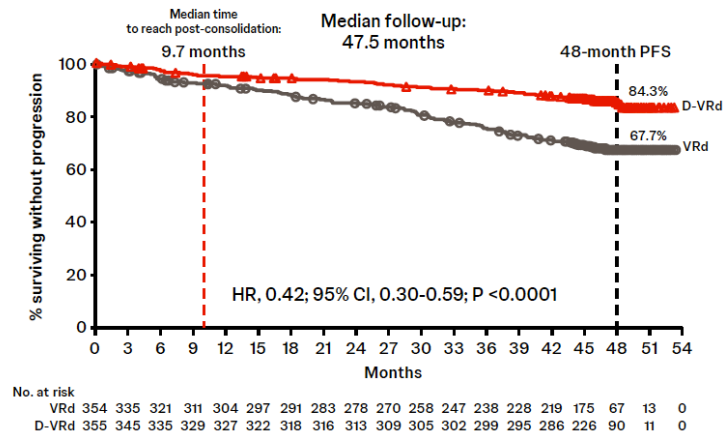
Moreau P. et al, EHA, 2024; Sonneveld P. et al, EHA, 2024

CASSIOPEIA

Median follow-up from first randomization: 80.1 months



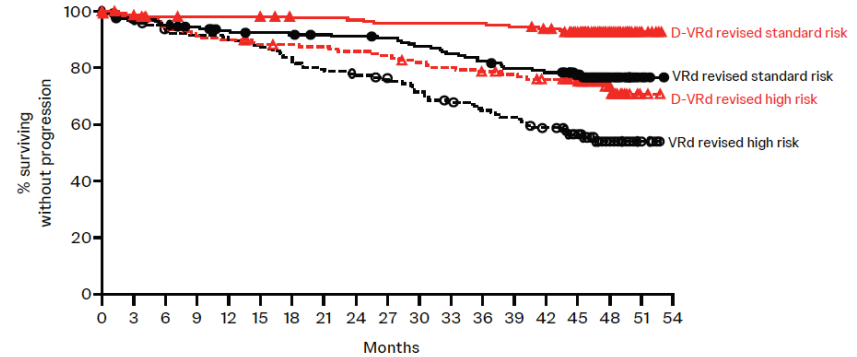
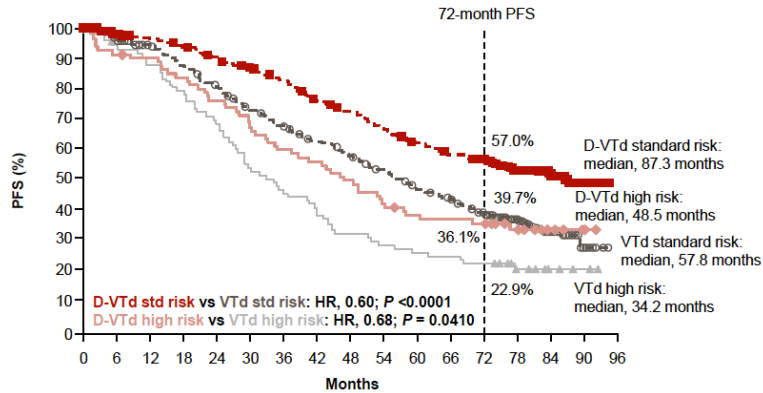
PERSEUS



Moreau P. et al, EHA, 2024; Sonneveld P. et al, EHA, 2024

CASSIOPEIA*

PERSEUS**



No. at risk	0	6	12	18	24	30	36	42	48	54	60	66	72	78	84	90	96
VTD std risk	454	424	402	373	341	308	284	259	239	217	190	174	150	91	43	10	0
VTD high risk	86	78	73	66	57	44	38	32	27	24	22	21	19	11	5	3	0
D-VTd std risk	460	437	427	416	397	379	359	329	311	288	265	248	231	140	76	15	0
D-VTd high risk	82	74	72	67	61	54	48	45	40	34	30	29	28	17	5	2	0

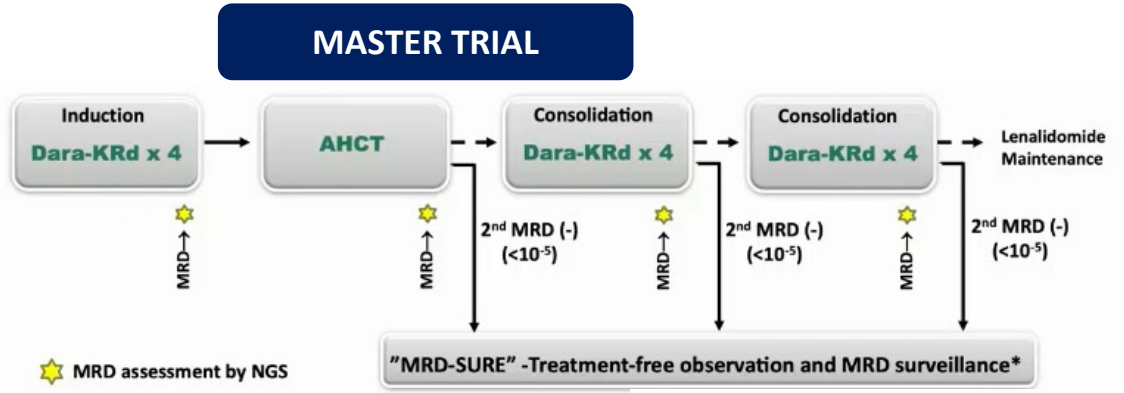
No. at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54
VRd revised standard risk	167	157	152	148	143	141	140	138	137	135	131	127	123	118	116	96	36	6	0
D-VRd revised standard risk	174	167	163	162	162	162	159	158	157	155	155	155	155	153	149	124	52	7	0
VRd revised high risk	148	139	132	129	127	123	118	112	109	105	98	92	87	84	77	64	22	4	0
D-VRd revised high risk	130	127	121	117	115	111	110	109	107	105	101	99	96	94	90	76	31	2	0

• HR=t(4;14) or del17p

** HR= t(4;14), del17p, gain1q or amp1q

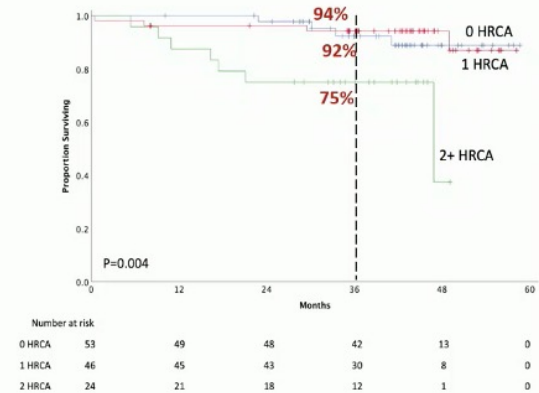
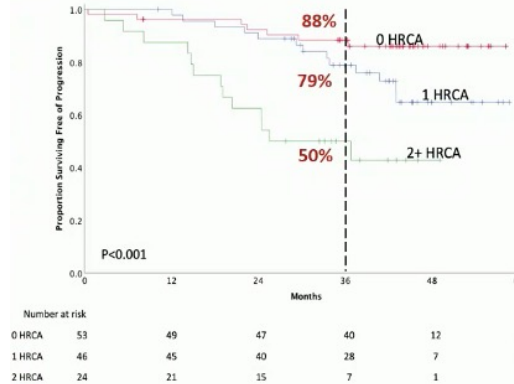
Corre J. et al, IMS, 2024; Dimopoulos M. et al, EHA, 2024

Convegno Regionale SIE



*24 and 72 weeks after completion of therapy

HRCA= *t(4;14); t(14,16), del17p, gain1q*



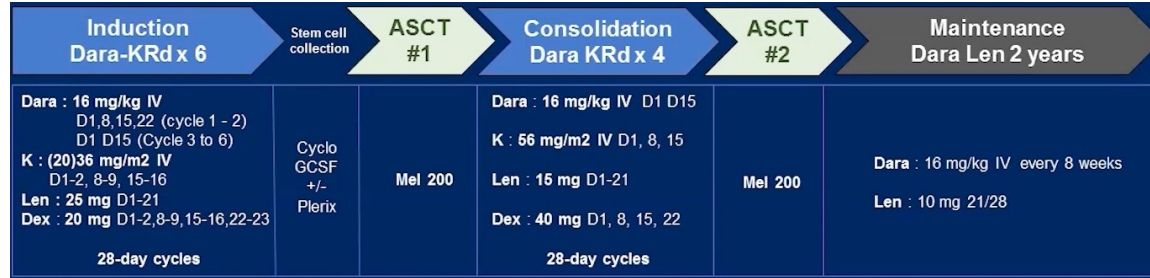
Costa L.J. et al, EHA; 2023

Convegno Regionale SIE

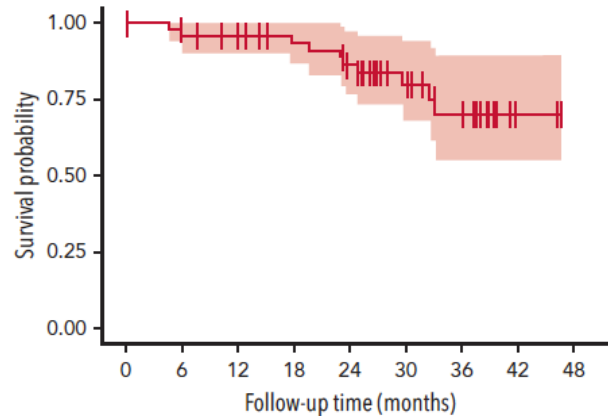


IFM-2018-04

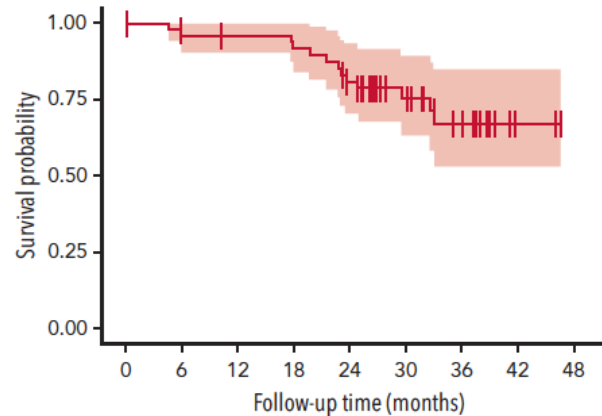
N=50
 HRCA= t(4;14); t(14,16),
 del17p



30 months PFS=81%

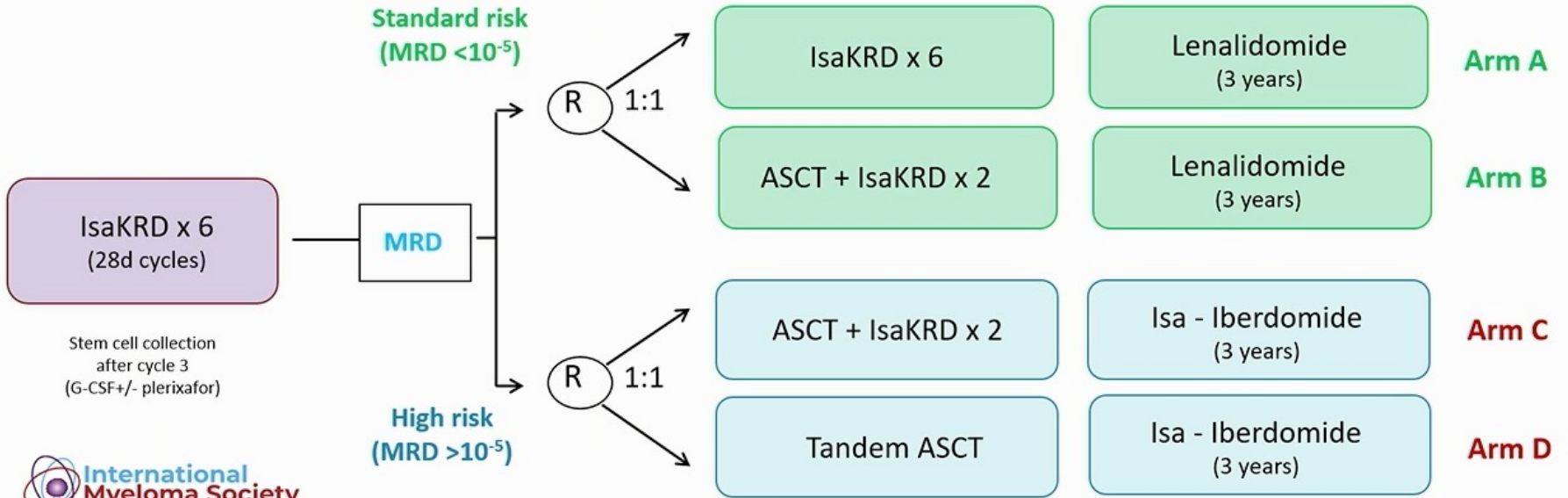


30 months OS=91%



Touzeau C. et al, Blood, 2024

MIDAS TRIAL

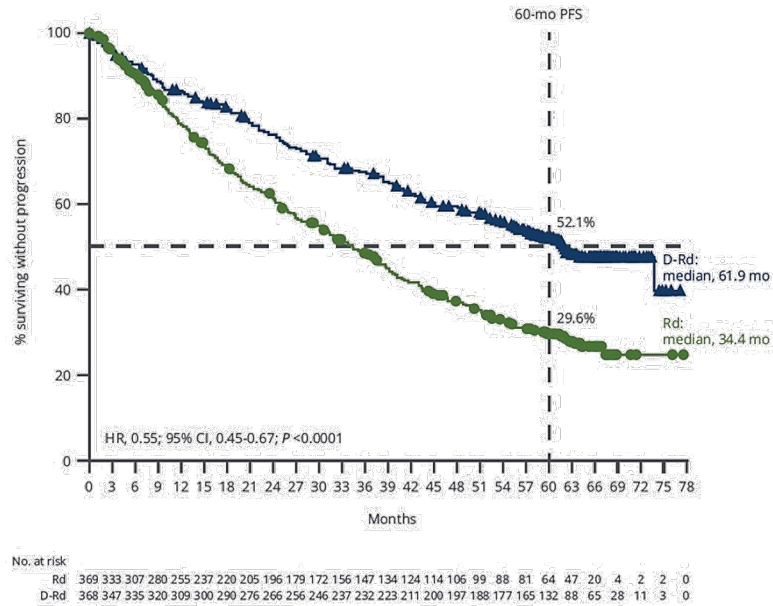


Perrot A. et al, IMS 2024

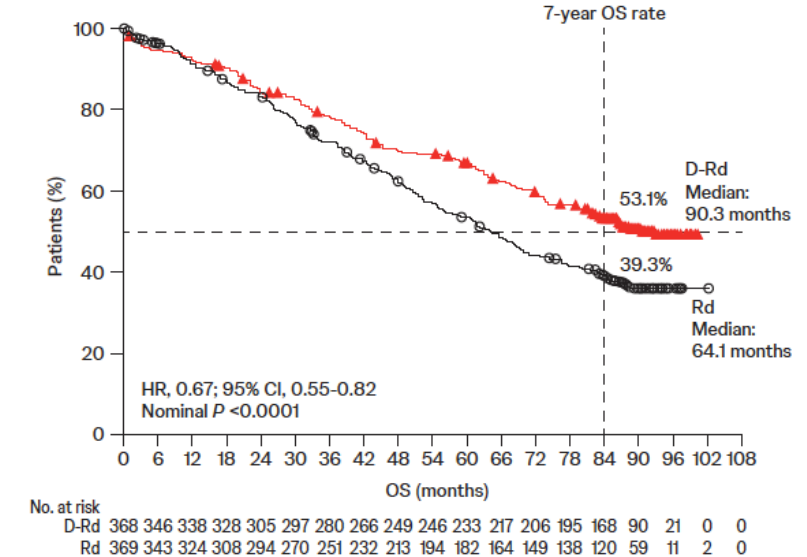
FINO A CHE ETA' PROPORRE ASCT?

MAIA

PFS



OS



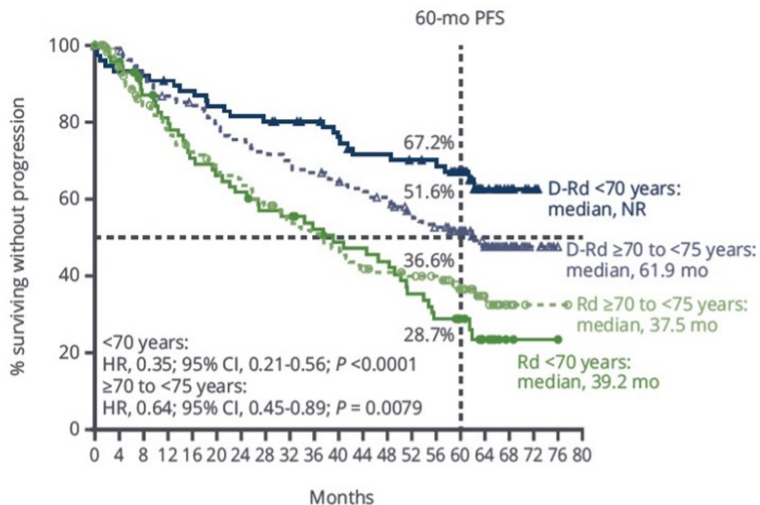
OS, overall survival; D-Rd, darunavir plus lenalidomide/dexamethasone; Rd, lenalidomide/dexamethasone; ITT, intent-to-treat; PFS, hazard ratio; CI, confidence interval.

*The ITT population included all randomized patients.

Kumar S. et al, ASH, 2022; Facon T. et al EHA, 2024

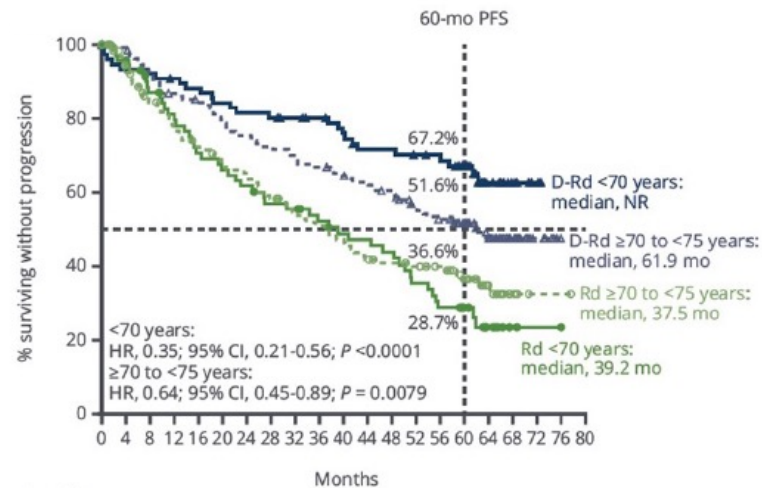
MAIA

PFS by age



No. at risk	77	70	59	53	47	44	41	37	36	32	29	28	26	21	17	13	7	2	1	1	0
Rd <70 years	77	70	59	53	47	44	41	37	36	32	29	28	26	21	17	13	7	2	1	1	0
D-Rd <70 years	78	72	71	69	67	64	62	61	59	57	54	49	49	47	45	38	19	10	2	0	0
Rd ≥70 to <75 years	131	115	99	89	83	77	74	66	60	56	52	46	43	41	38	28	15	5	1	1	0
D-Rd ≥70 to <75 years	130	127	118	110	106	100	95	91	88	84	81	77	73	64	59	48	33	18	6	0	0

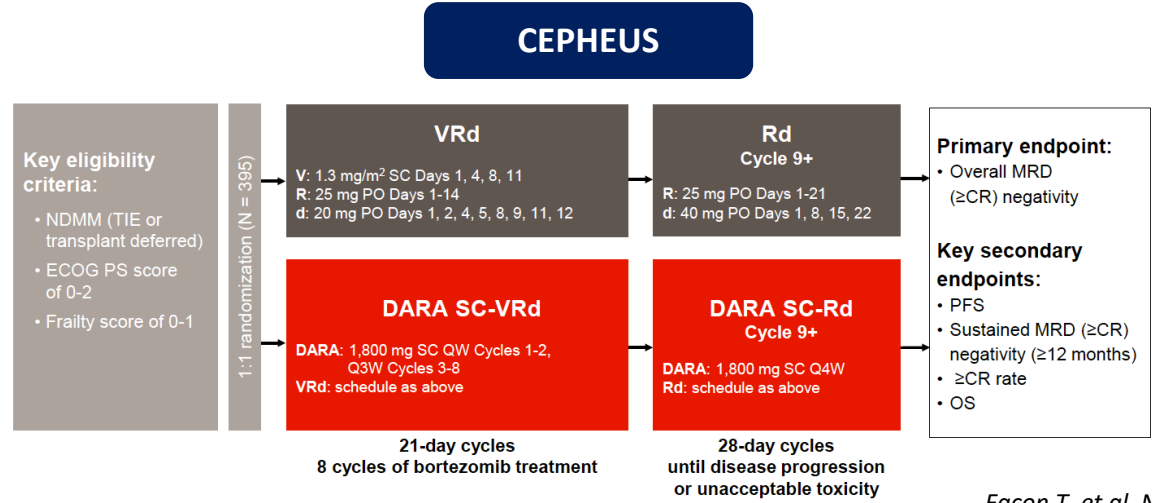
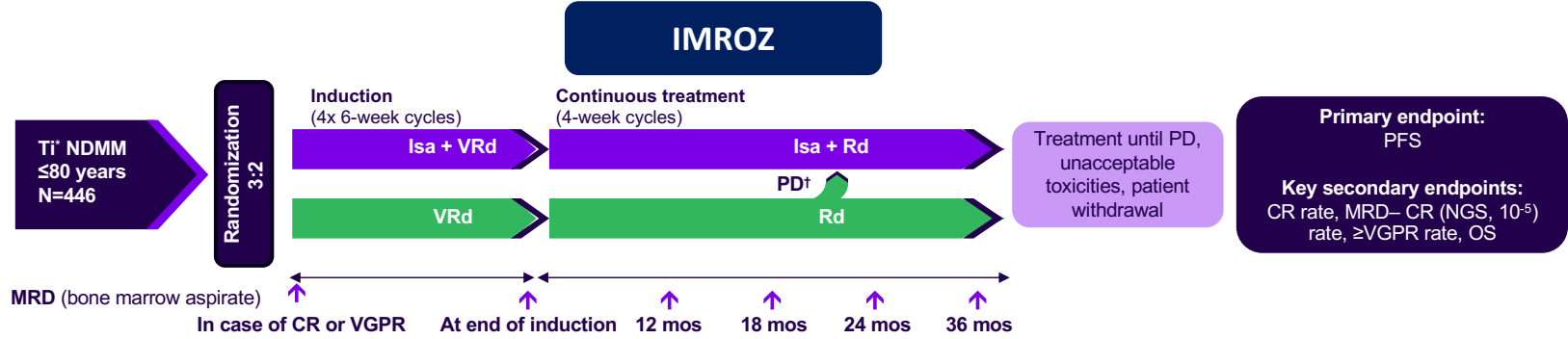
OS by age



No. at risk	77	70	59	53	47	44	41	37	36	32	29	28	26	21	17	13	7	2	1	1	0
Rd <70 years	77	70	59	53	47	44	41	37	36	32	29	28	26	21	17	13	7	2	1	1	0
D-Rd <70 years	78	72	71	69	67	64	62	61	59	57	54	49	49	47	45	38	19	10	2	0	0
Rd ≥70 to <75 years	131	115	99	89	83	77	74	66	60	56	52	46	43	41	38	28	15	5	1	1	0
D-Rd ≥70 to <75 years	130	127	118	110	106	100	95	91	88	84	81	77	73	64	59	48	33	18	6	0	0

Facon T. et al ASH, 2022

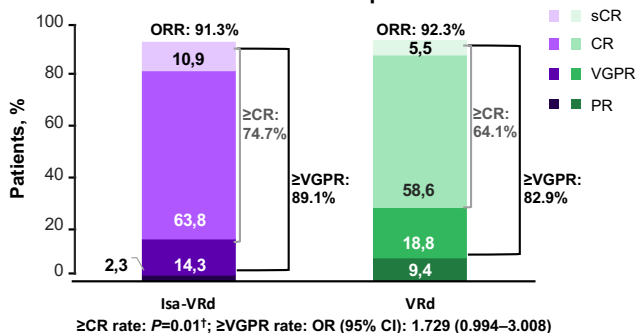
Convegno Regionale SIE



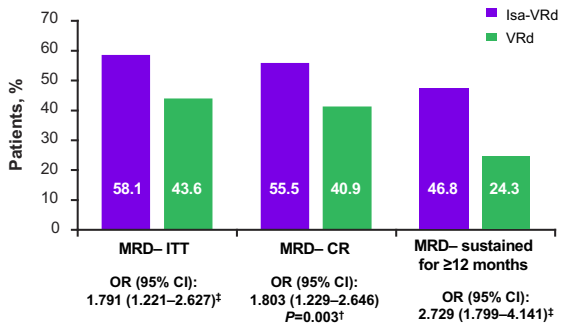
Facon T. et al, NEJM, 2024; Usmani S. et al, IMS, 2024

IMROZ

Best Overall Response

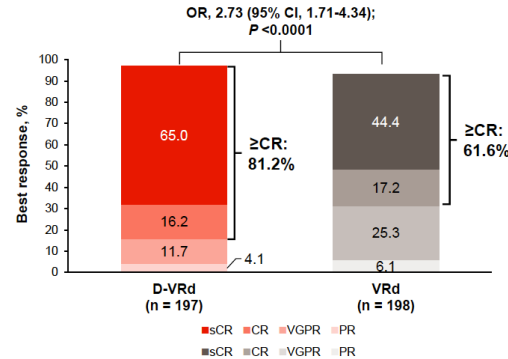


MRD Rate (NGS, 10^{-5})

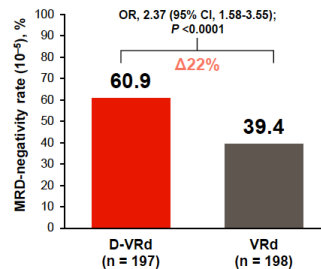


CEPHEUS

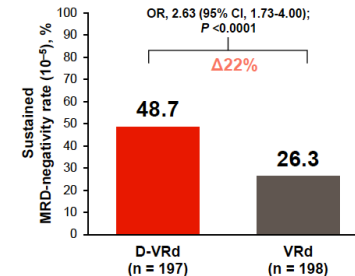
≥CR rate



Primary endpoint Overall MRD-negativity rate (10^{-5})

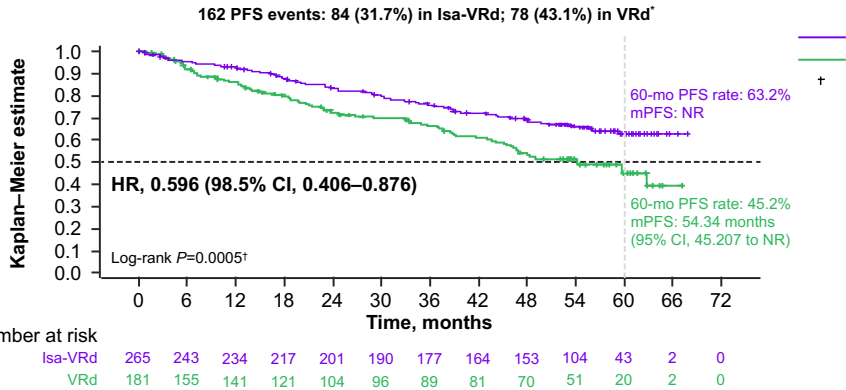


Sustained MRD-negativity rate (10^{-5}) ≥12 months

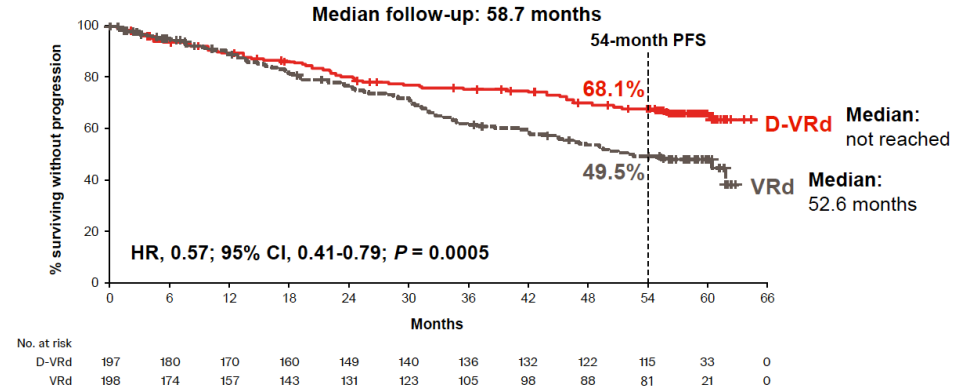


Facon T. et al, NEJM, 2024; Usmani S. et al, IMS, 2024

IMROZ



CEPHEUS



Facon T. et al, NEJM, 2024; Usmani S. et al, IMS, 2024

TOSSICITA' SECONDARIE A ASCT?

GIMEMA MMY-3006

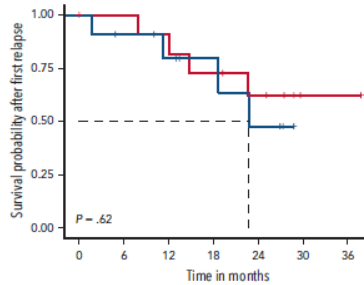
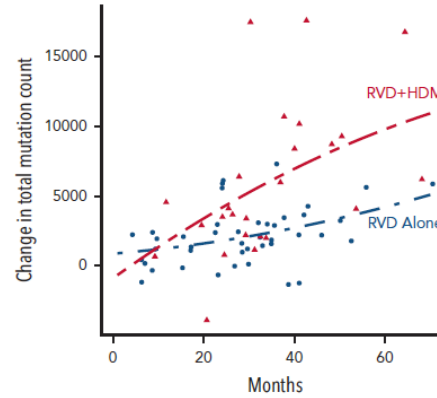
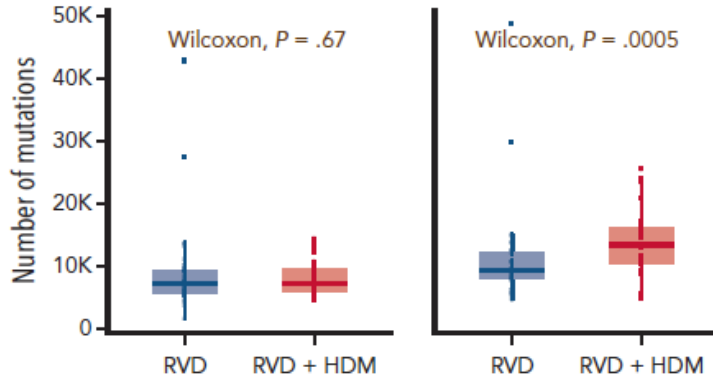
SPMs	VTD (n=233)	TD (n=218)	P-value
All SPMs, incidence per 100/person-years	0.87 (95% CI 0.49-1.44)	1.41 (95% CI 0.88-2.13)	0.26
All SPMs, n (%)	15 (6)	22 (10)	0.17
Hematologic, n (%)	4 (2)	6 (3)	
-AML	2	2	
-MDS	2	0	
-NHL	0	4	
Solid tumor, n (%)	11 (5)	16 (7)	
-non-skin	8	12	
-skin	3	4	

EMN02/HO95

	OVERALL 1493	Transplantation 707	VMP 495	p-value
Patients with SPM, n (%)	86 (5.8)	42 (6.0)	31 (6.3)	0.903
Haematologic malignancies	22 (1.5)	12 (1.7)	9 (1.8)	0.748
Acute leukemias	7	3	4	
Lymphomas	3	2	1	
Myelodysplastic syndromes	12	7	4	
Incidence rate (x100pts-yr)	1.4	1.44	1.54	0.875
95 CI	(1.12-1.72)	(1.05-1.95)	(1.05-2.18)	
Time to SPM development	55.6	54.50	52.50	0.260
median (IQR)	33.5-66.2	40.45-63.98	37.95-62.70	

Tacchetti P. et al Lancet Haematol. 2020 ; Cavo M. et al Lancet Haematol, 2020

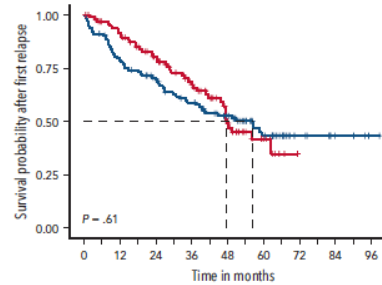
Convegno Regionale SIE



	0	6	12	18	24	30	36
Strata < Median	12	11	10	8	5	1	1
Strata > Median	11	9	7	5	3	0	0

Number at risk

Time in months



	0	12	24	36	48	60	72	84	96							
CR/SCR	100	91	86	76	67	55	48	36	25	15	10	2	0	0	0	0
Other Response	114	103	88	82	73	64	59	51	46	34	25	18	10	8	4	4

Number at risk

Time in months

Samur M.K. Et al, Blood, 2023

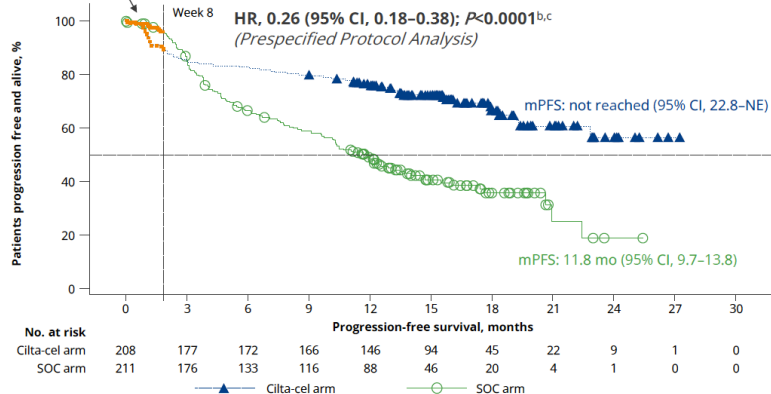
QUAL E' IL FUTURO DEL TRAPIANTO AUTOLOGO?

Cartitude 4

Bridging phase, patients in cilta-cel arm were receiving the same treatment as the SOC arm

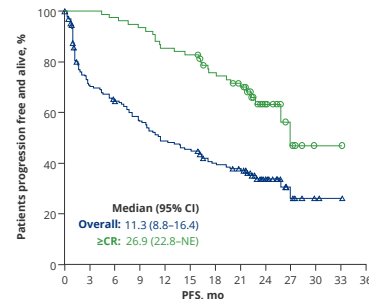
Progression-free survival^a

HR, 0.26 (95% CI, 0.18-0.38); $P < 0.0001$ ^{b,c}
(Prespecified Protocol Analysis)

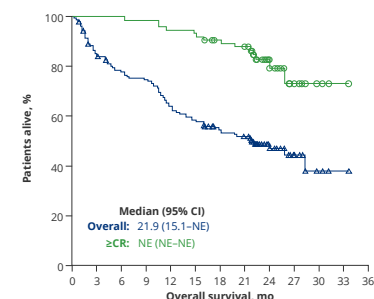


MajesTEC-1

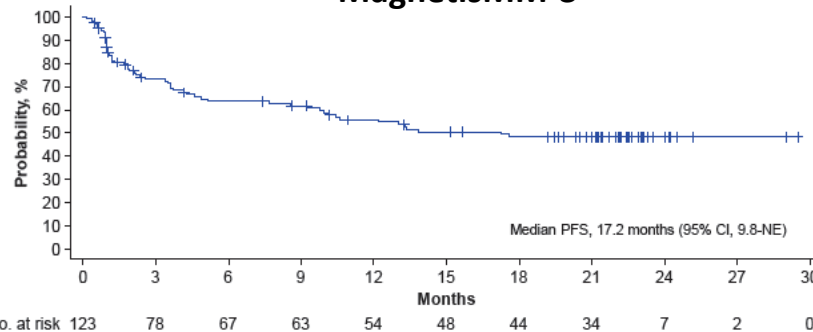
Progression-free survival



Overall survival

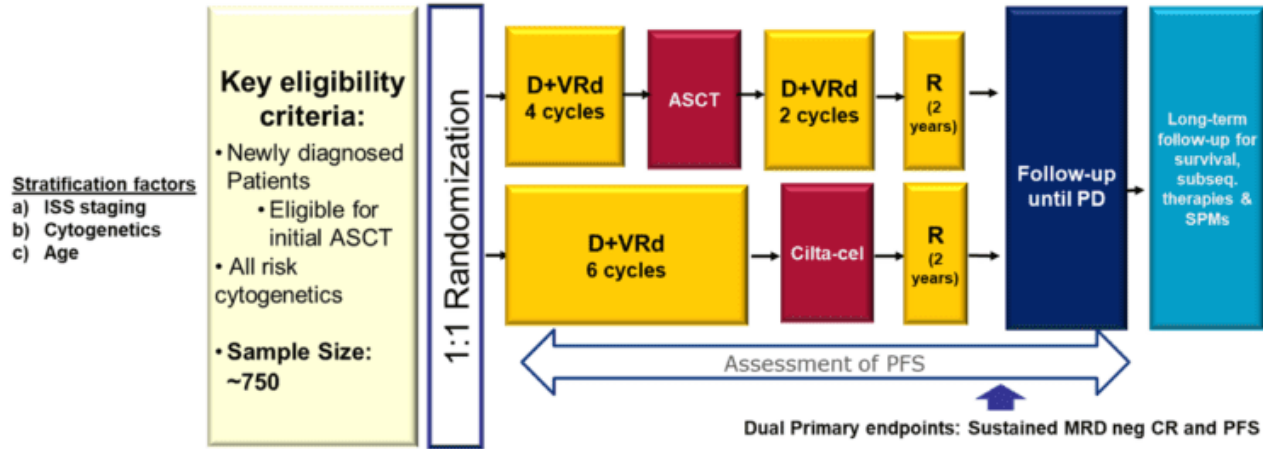


MagnetisMM-3

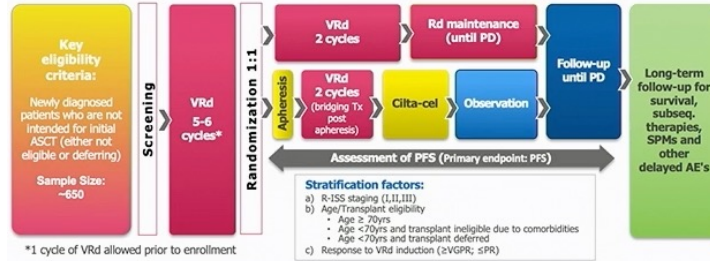


San Miguel et al, NEJM, 2023; Van de Donk et al, ASCO, 2023; Tomasson M. et al, ASH, 2023

EMN28/ CARTITUDE-6



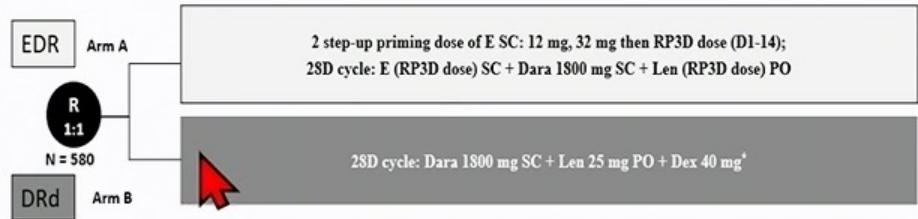
CARTITUDE-5 (NTE fit)



MAJESTEC-7: phase 3 (n = 1500)



MAGNETISMM-6: phase 3 (n = 580)



- ASCT in prima linea rimane lo standard of care per il paziente TE (PFS)
- In casi selezionati si può pensare a ASCT in recidiva (OS)
- Il tandem ASCT sembra garantire outcome migliori nell'alto rischio citogenetico → ruolo del tandem ASCT meno chiaro nell'era delle quadruplette
- In pazienti età >65 anni con comorbidità o che rifiutano ASCT si può proporre D-RD (a breve Isa-VRD/D-VRD?)
- Domande aperte?
 - età limite ASCT: 70?, 65?
 - tossicità a lungo termine
 - ruolo di CAR-T e bispecifici

Convegno Regionale SIE



GRAZIE PER L'ATTENZIONE!