ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA
DIPARTIMENTO DI
SCIENZE MEDICHE E CHIRURGICHE

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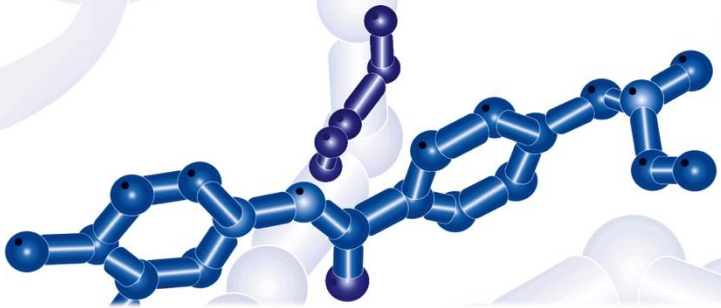

New Drugs in Hematology

Multiple Myeloma

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Bologna,
Royal Hotel Carlton
May 18-19-20, 2026

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Amgen	X						
AbbVie	X		X			X	
Astra Zeneca	X						
BMS	X		X			X	
Kite/Arcellx			X			X	
Roche-Genentech	X		X			X	
Sanofi	X		X			X	

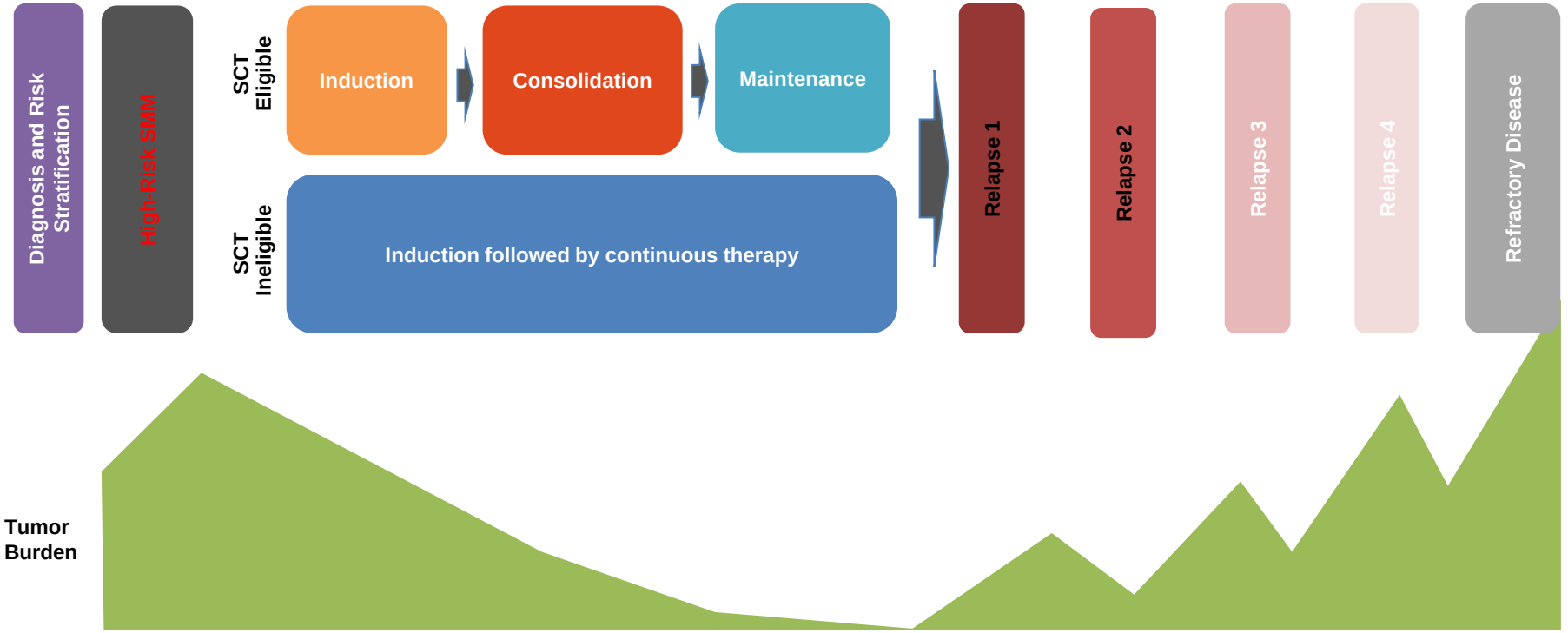
Sodoku…and myeloma?

Sudoku is a logic-based number puzzle where the goal is to fill a 9x9 grid with digits (1–9). Each row, column, and 3x3 sub-grid must contain all the digits without any repetitions.

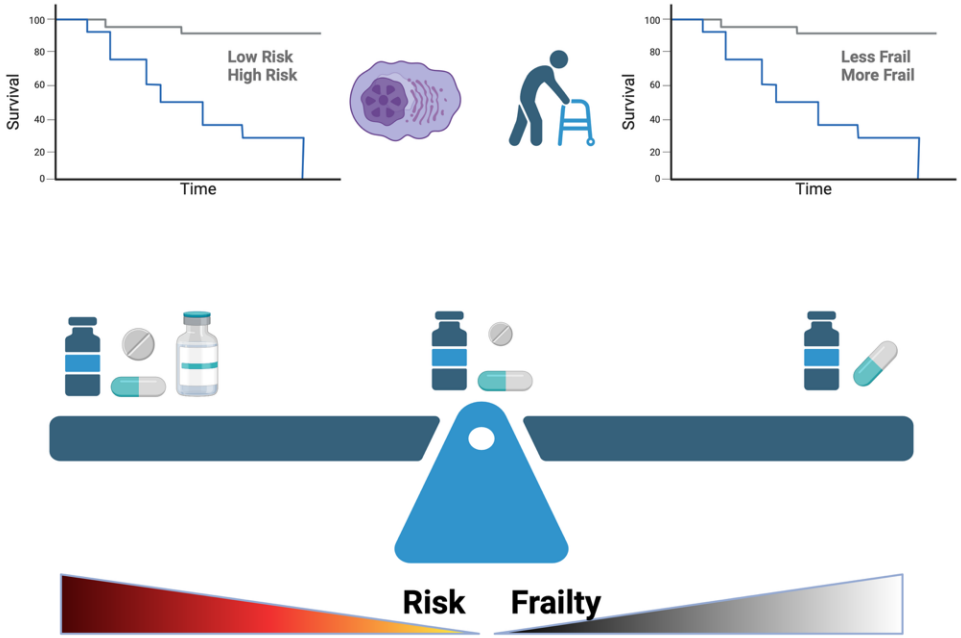
Building blocks…adds up to same goal

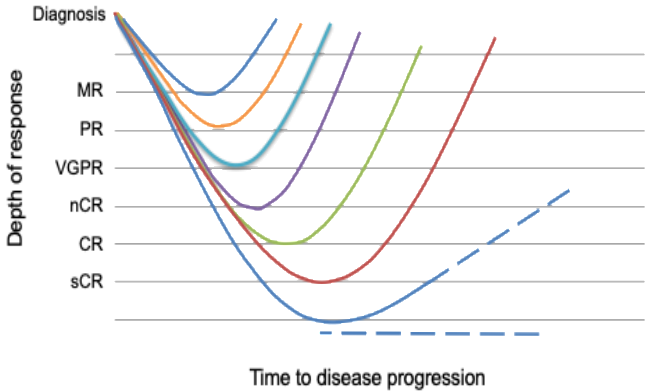
	Class	Drugs
1	IMiDs	Lenalidomide, pomalidomide
2	Proteasome inhibitors	Bortezomib, carfilzomib, ixazomib
3	Anti-CD38 MoAb	Daratumumab, isatuximab
4	Anti-SLAMF7 MoAb	Elotuzumab
5	Bispecific antibodies	Teclistamab, elranatamab, linvoseltamab, talquetamab
6	CART	Idecel, ciltacel
7	ADC	Belantamab
8	Chemotherapy	Melphalan, Cytoxan, doxorubicin, etoposide, cisplatin, bendamustine
9	ASCT	HD melphalan and stem cells

Myeloma Treatment Paradigm



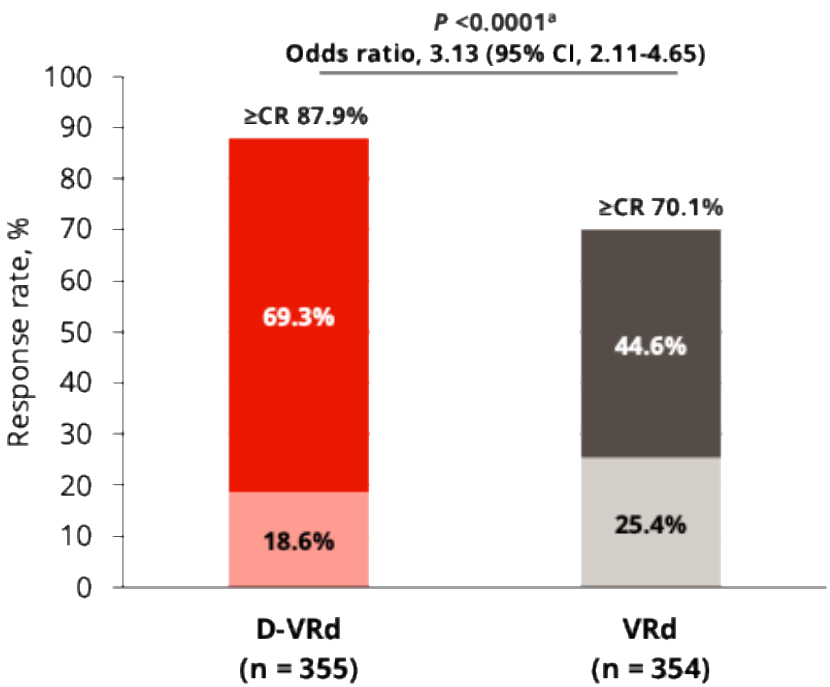
What drives the treatment decisions?

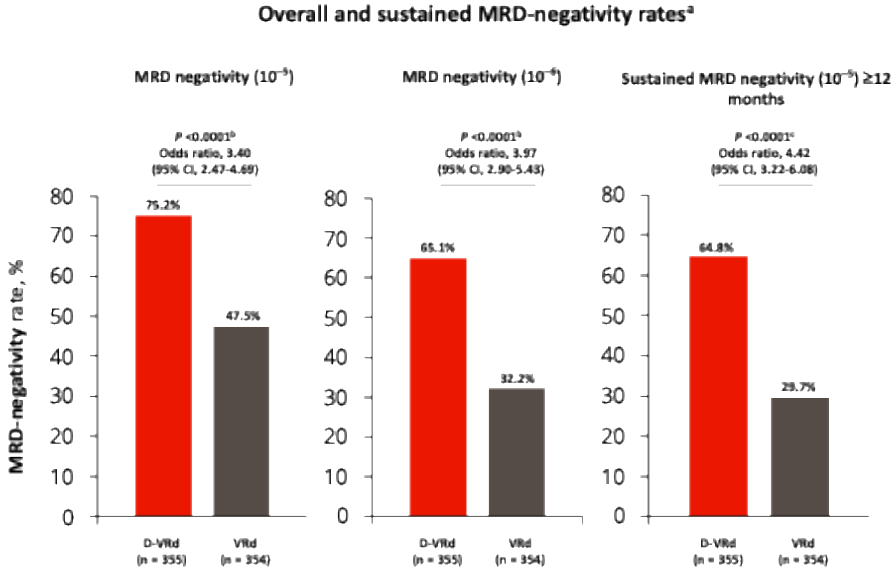




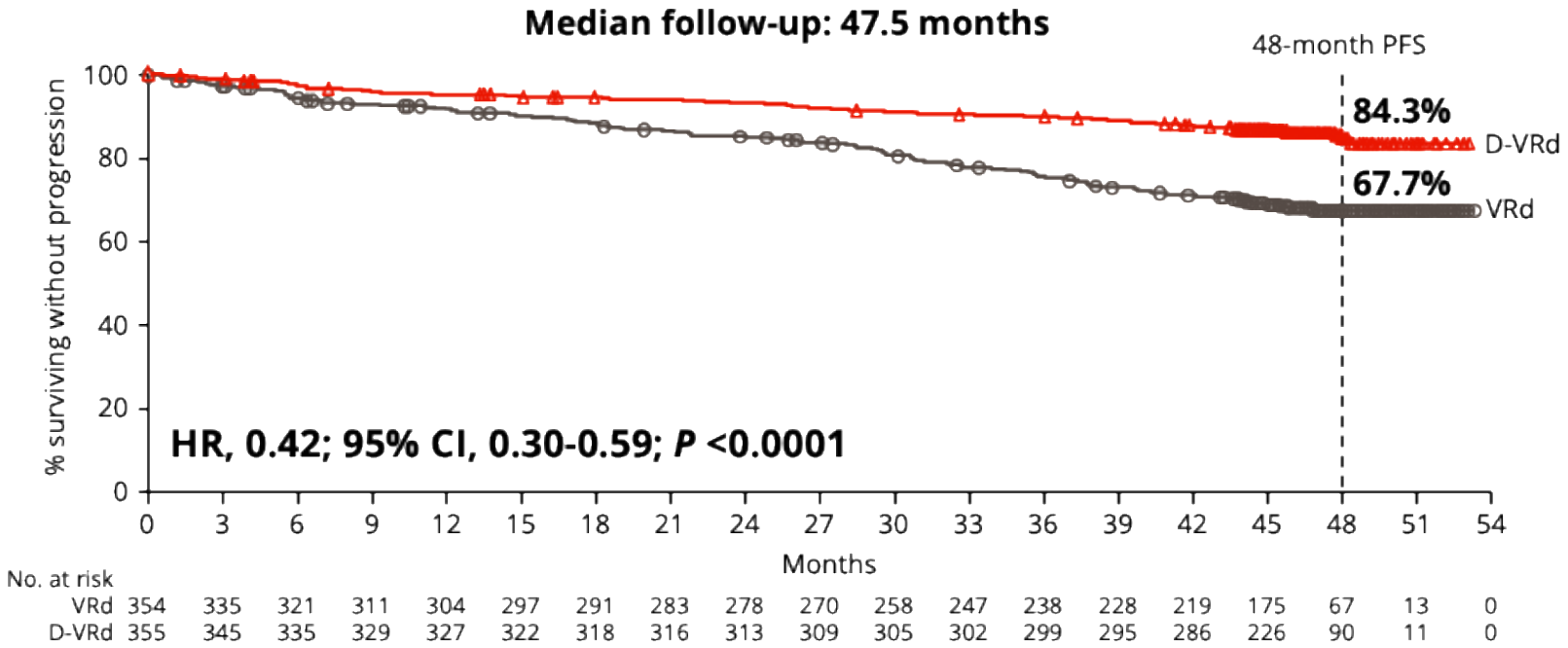
Newly Diagnosed MM-ASCT eligible

PERSEUS – Daratumumab +VRd vs VRd

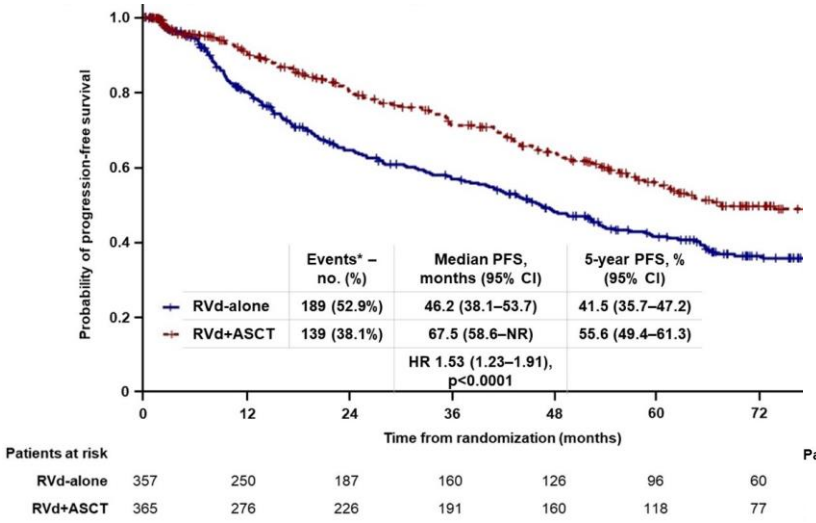


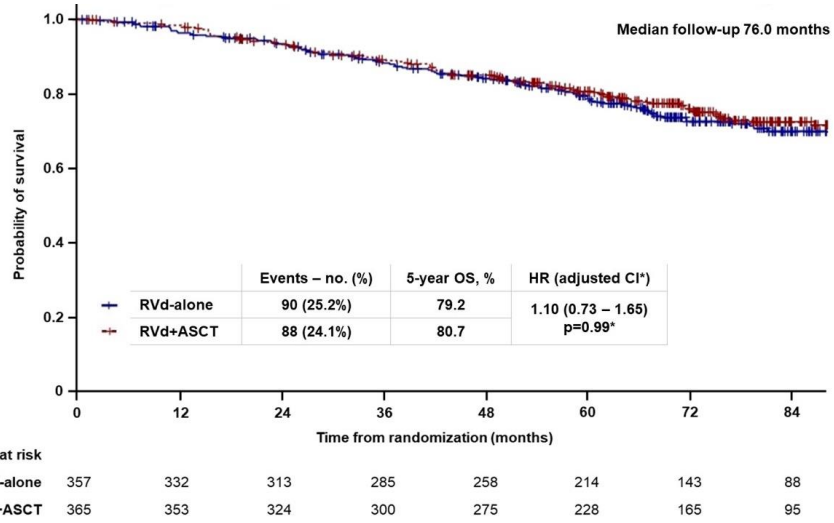


PERSEUS – Progression Free Survival



DETERMINATION: Role of ASCT

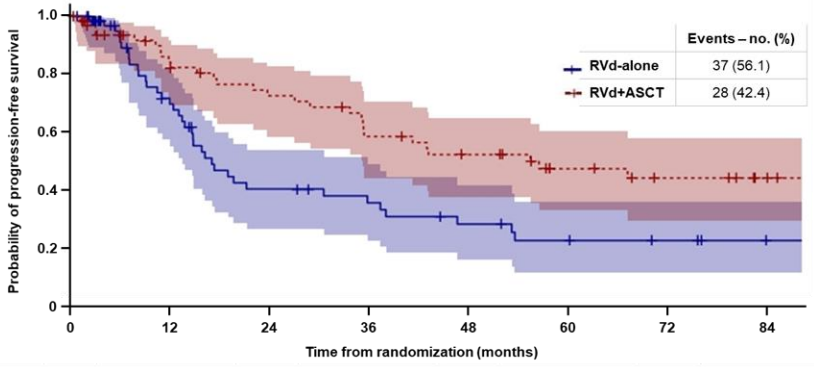




Paul Richardson et al

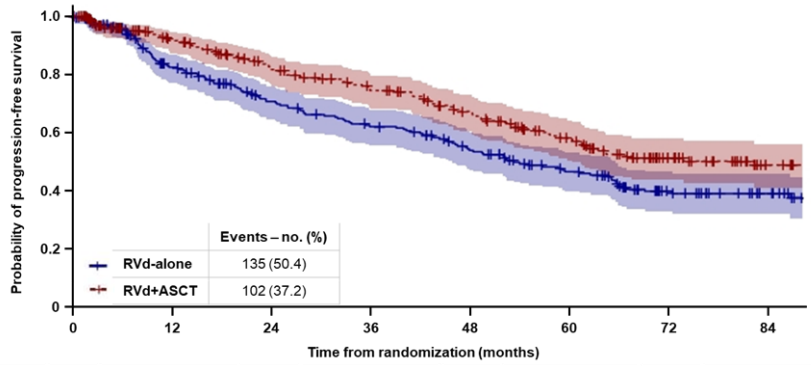
DETERMINATION - PFS by cytogenetic risk

Median PFS, months	RVd-alone	RVd+ASCT
High-risk	17.1	55.5
	HR 1.99 (95% CI 1.21–3.26)	



Patients at risk								
RVd-alone	66	36	19	16	11	8	6	3
RVd+ASCT	66	45	37	29	24	16	12	8

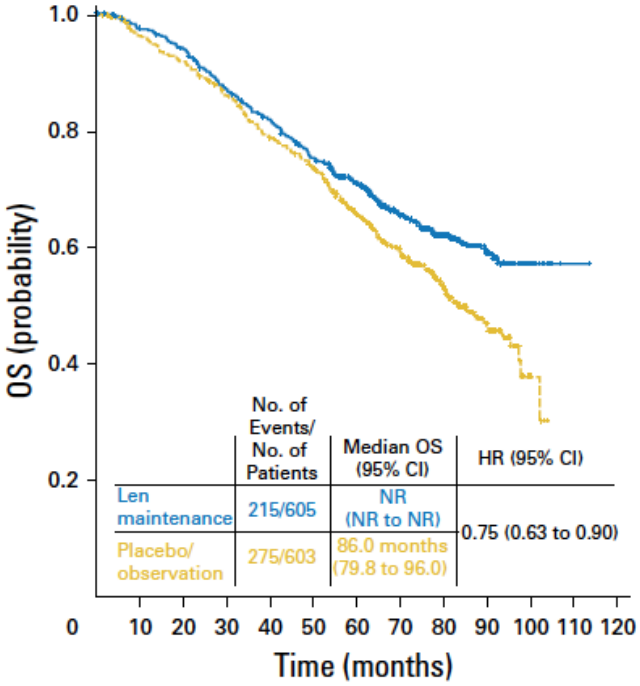
Median PFS, months	RVd-alone	RVd+ASCT
Standard-risk	53.2	82.3
	HR 1.38 (95% CI 1.07–1.79)	

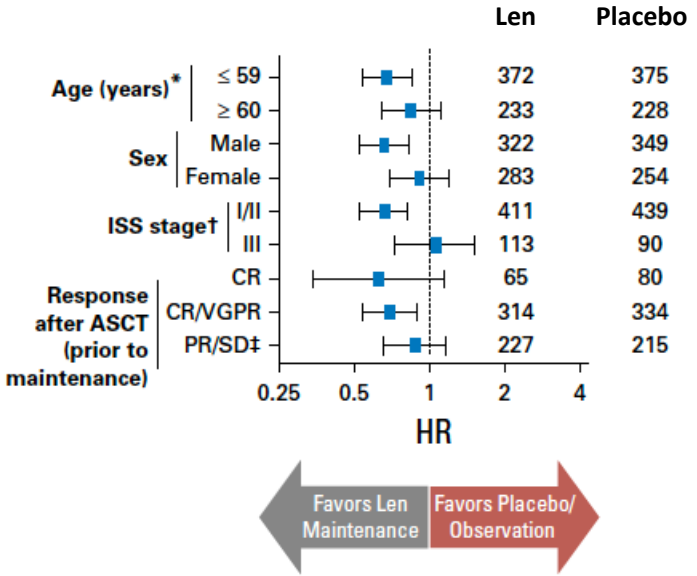


Patients at risk								
RVd-alone	268	197	156	134	109	83	50	34
RVd+ASCT	274	212	175	151	126	94	58	29

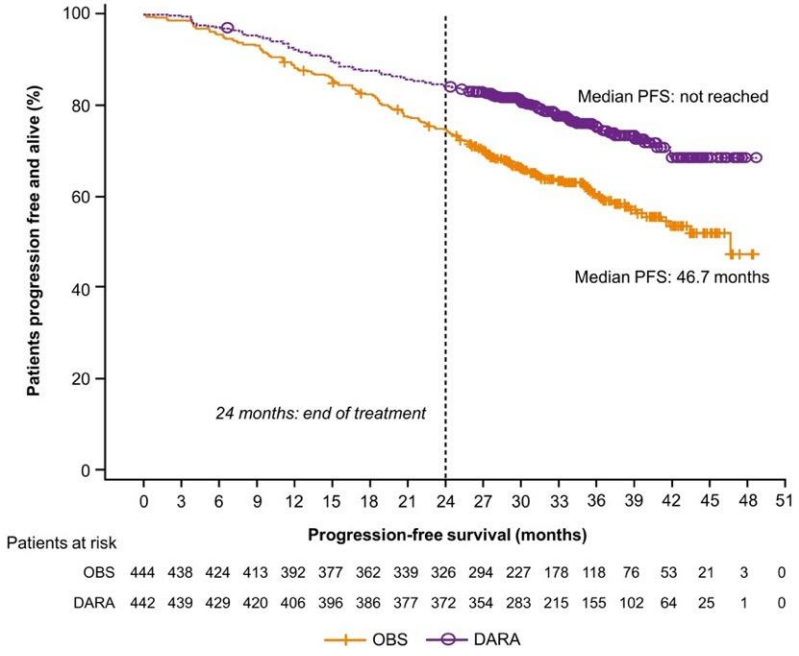
Paul Richardson et al

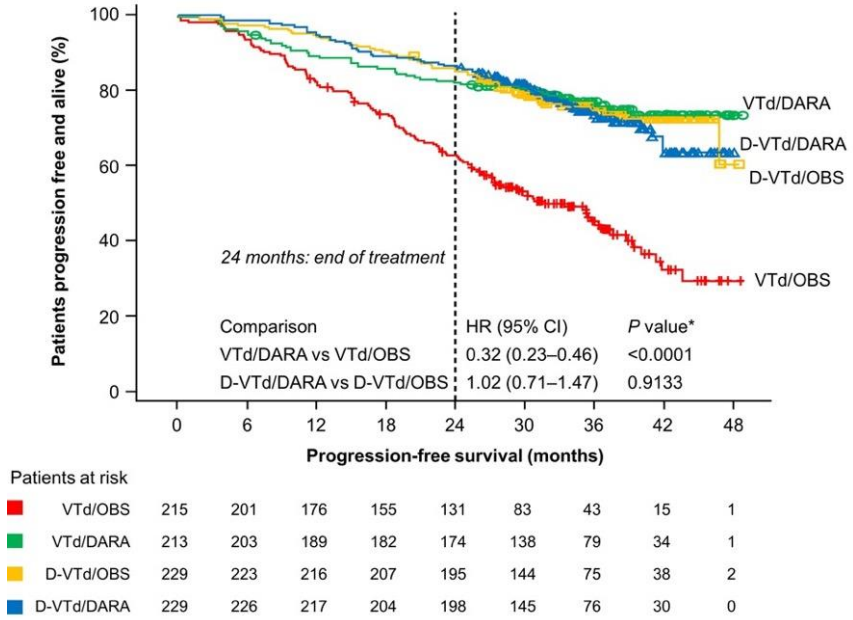
Lenalidomide maintenance





Daratumumab maintenance: Cassiopeia



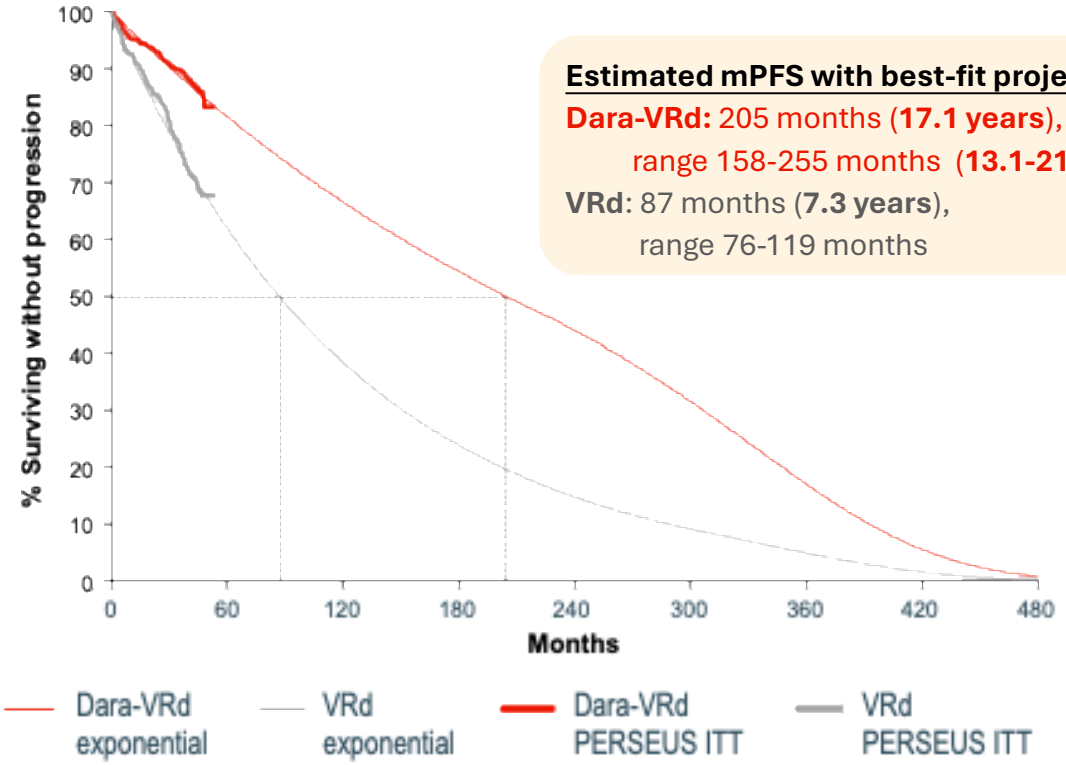


Other quadruplets in induction pre-SCT

Regimen	Induction VGPR	Best VGPR	MRD	PFS
Dara-VTd	65%	84%	65.1%	83.7 mos
Dara-KRd	88%	98%	81%	3yr ~ 80%
Isa-VRd	77%	-	-	3 yr PFS ~ 83%
Isa-KRd	84%	90%	82%	NA

Predicted PFS

D/I	R	V/K
S	C	T
D	-	R



Estimated mPFS with best-fit projections:

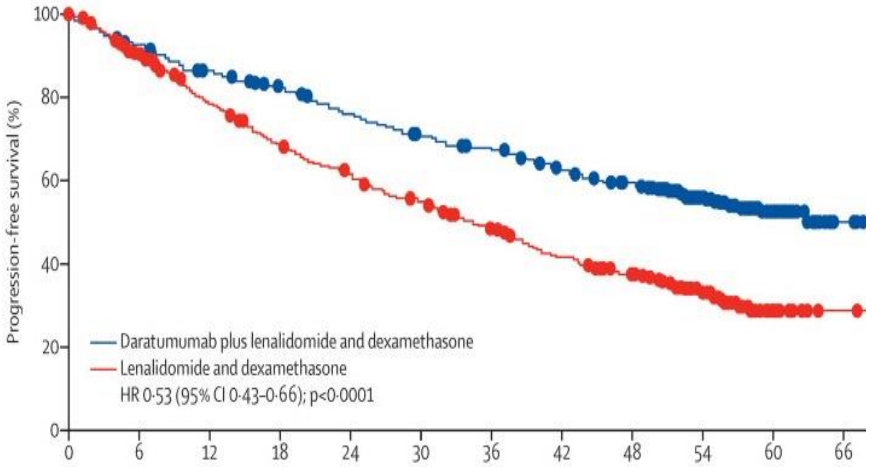
Dara-VRd: 205 months (**17.1 years**),
range 158-255 months (**13.1-21.3 years**)

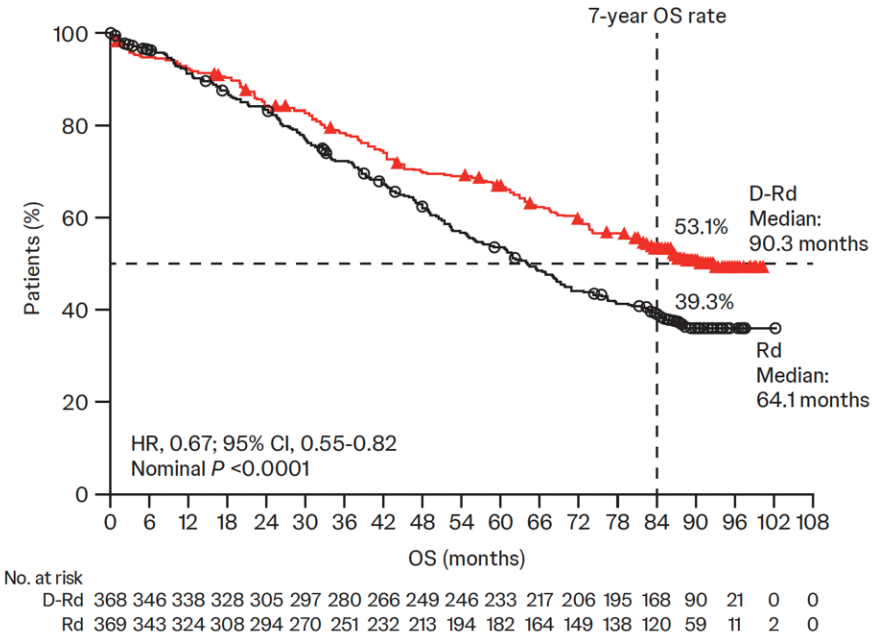
VRd: 87 months (**7.3 years**),
range 76-119 months

Sonneveld et al. EMN 2025; Abstract No. B04

Newly Diagnosed MM-ASCT ineligible

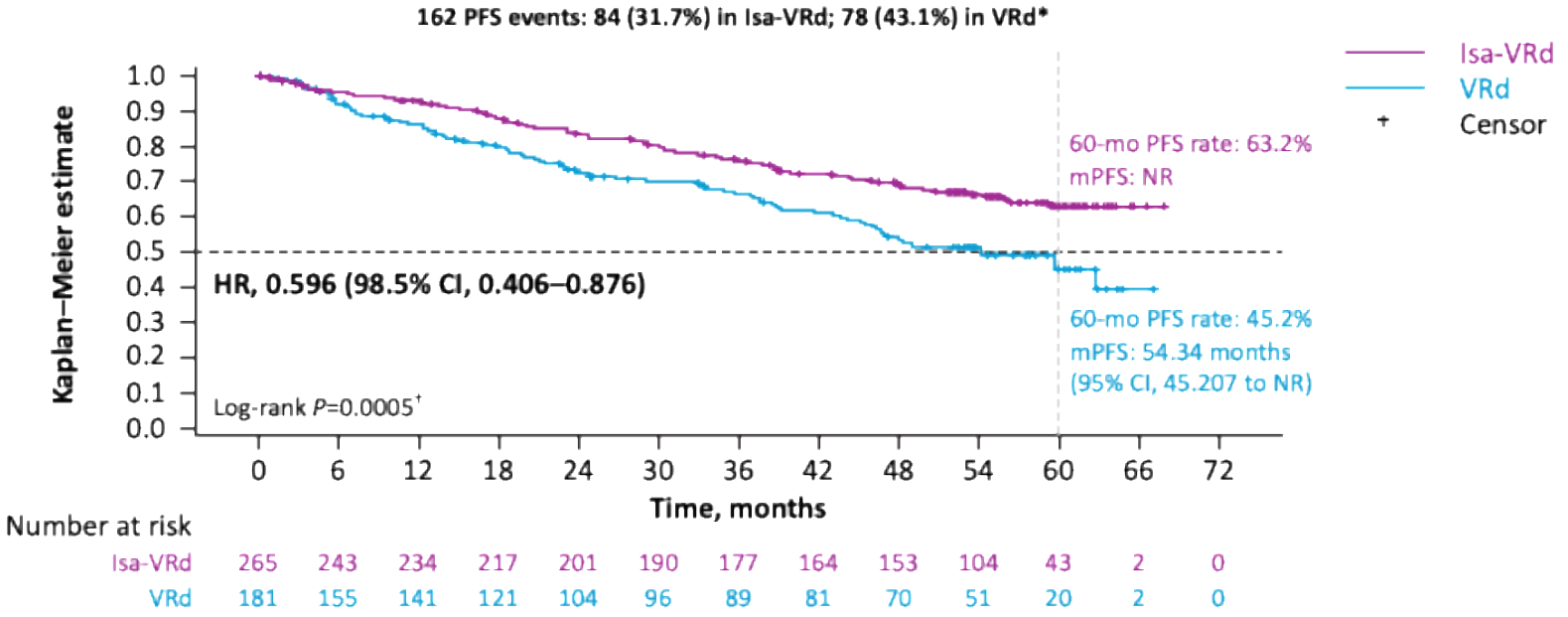
MAIA – Daratumumab – Len-dex (DRd)





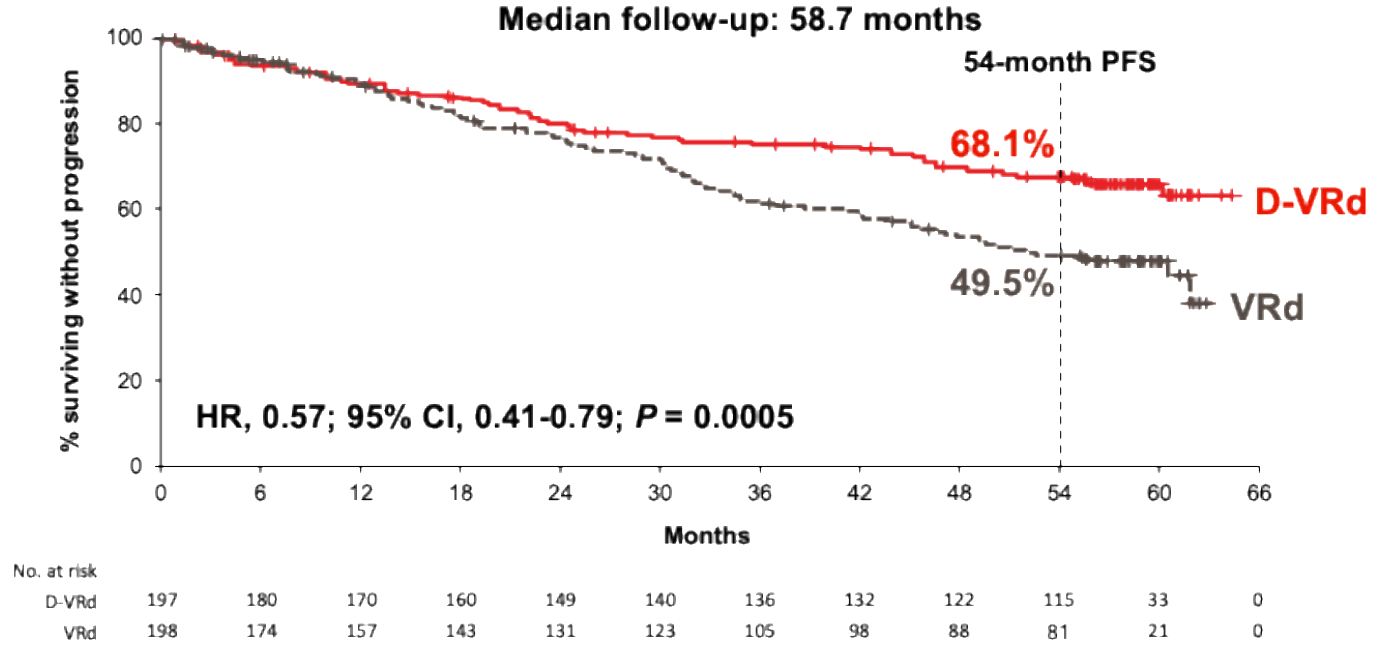
Facon et al, Lancet Oncol 2021; 22: 1582–96

IMROZ – Progression Free Survival



Facon et al, ASCO 2024

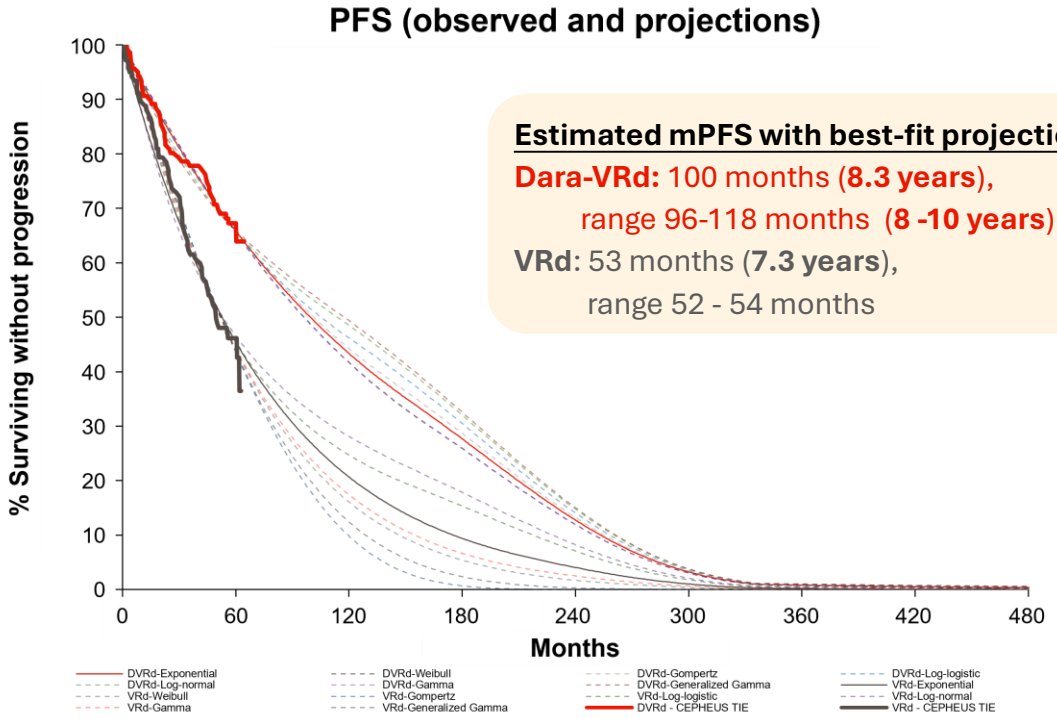
CEPHEUS – Progression free survival



Usmani et al, IMS Annual Meeting, 2024

Predicted PFS

D/I	R	Vd
D/I	R	Vd
D/I	-	R

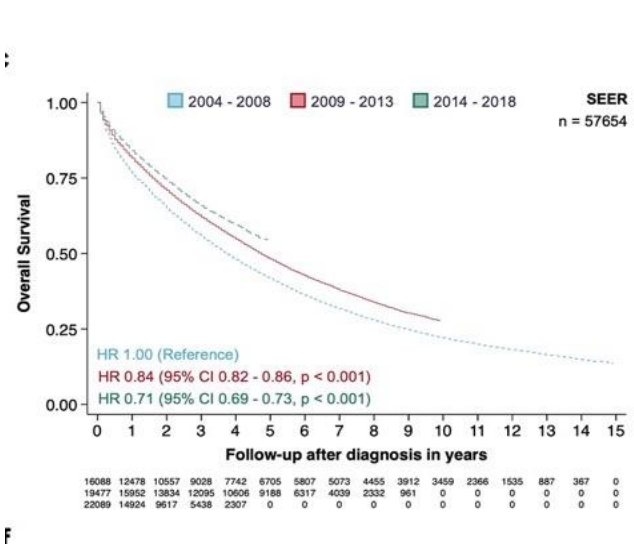


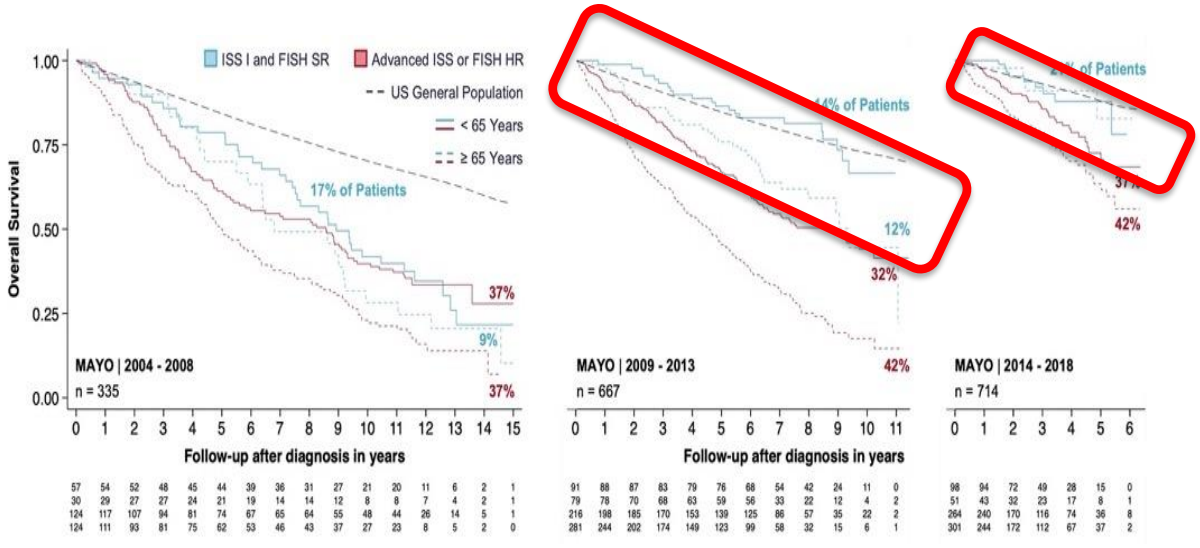
Estimated mPFS with best-fit projections:

Dara-VRd: 100 months (**8.3 years**),
range 96-118 months (**8 -10 years**)

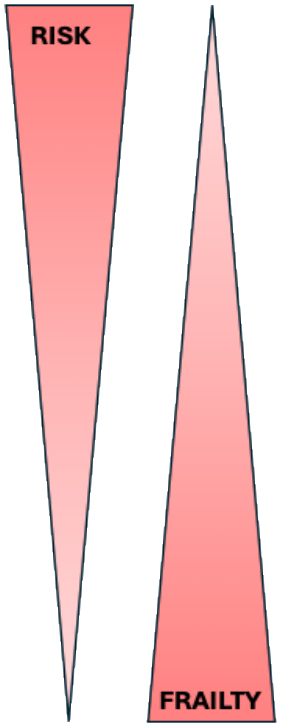
VRd: 53 months (**7.3 years**),
range 52 - 54 months

And we already a functional cure in some…





Individualizing the treatment approach



QUADRUPLET

TRIPLET

ASCT

-if eligible and desired

Doublet maintenance

Single drug maintenance

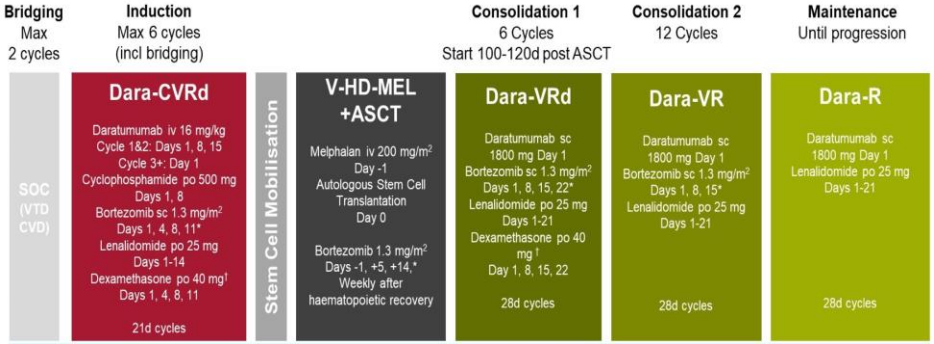
Doublet maintenance

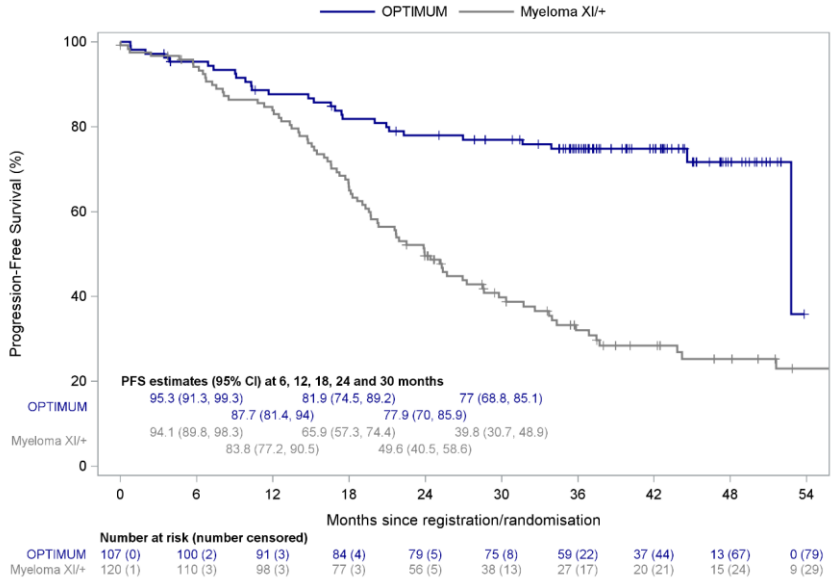
DOUBLET (add 3rd drug if tolerated)

Single drug maintenance

How long?

High risk MM -OPTIMUM Trial





Relapsed MM

Approach to first relapse

ASCT

→ Len maintenance

→ Dara/Len maintenance

→ Btz/Len maintenance

Anti-CD38 + Len Dex→ Dara/Len maintenance

Anti-CD38 + VRd→ Dara/Len maintenance

Btz Len Dex→ Len maintenance

Len Dex→ Len maintenance

Len refractory/ Anti-CD38 sensitive

Anti-CD38 refractory/ Len sensitive

Anti-CD38 + Len refractory

Anti-CD38 + Len sensitive

Anti-CD38 combinations

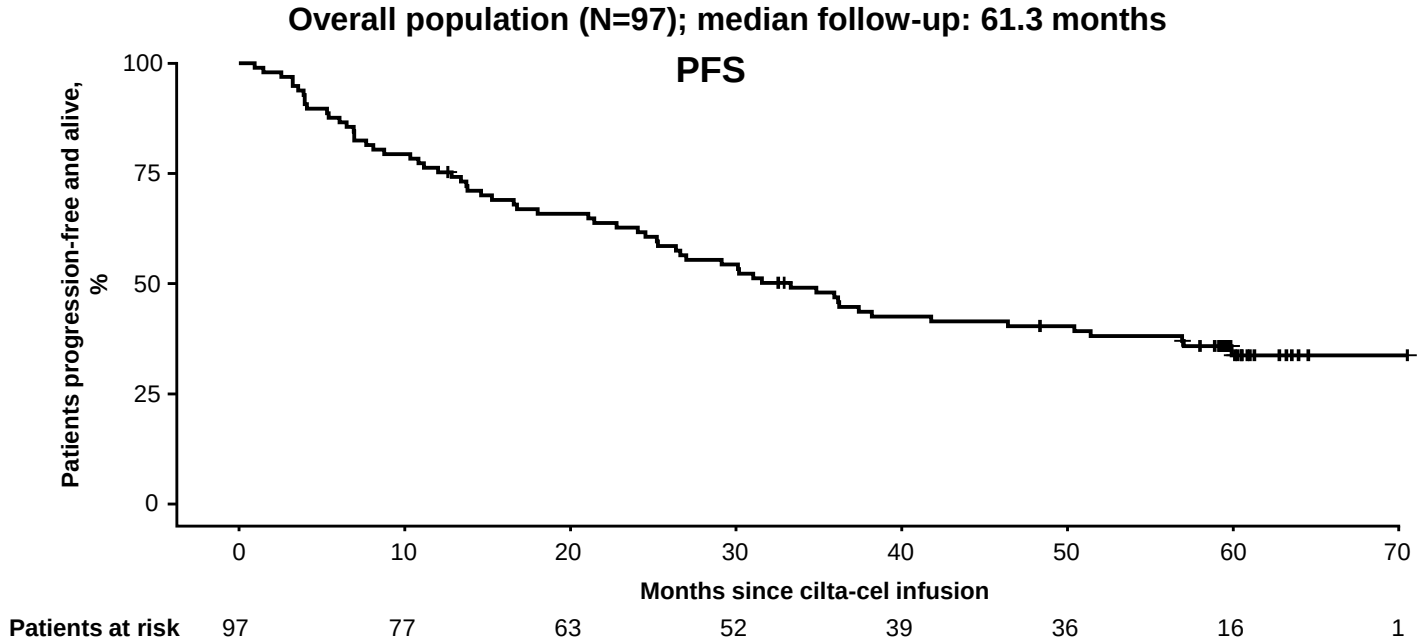
Trial	Design	Median PFS	Response
CANDOR	**D-Kd** vs Kd	28.4 vs 15.2 mo; HR 0.64	ORR 84.3% vs 74.7%
IKEMA	**Isa-Kd** vs Kd	35.7 vs 19.2 mo; HR 0.58	sCR/CR 44.1% vs 28.5%
ICARIA-MM	**Isa-Pd** vs Pd	11.5 vs 6.5 mo; HR 0.596	ORR 60.4% vs 35.3%
APOLLO	**D-Pd** vs Pd	12.4 vs 6.9 mo; HR 0.63	ORR 68.9% vs 46.4%

D-Daratumumab, Isa-Isatuximab, K-Carfilzomib, d-dexamethasone

CART

CAR-T product	Key trial / population	Response rate	Survival / durability
Idecabtagene vicleucel	KarMMa, single-arm phase 2; RRMM; n=128	**ORR 73%;** ≥CR 33%	Median PFS ~ 8.6–8.8 mo; median OS ~ 24.8 mo.
Idecabtagene vicleucel	KarMMa-3, phase 3; triple-class–exposed RRMM after 2–4 prior regimens	**ORR 71%** vs 42%; CR 44% vs 5%	Median PFS 13.8 mo vs 4.4 mo, HR 0.49. Median OS 41.4 mo vs 37.9 mo (56% crossover to ide-cel).
Ciltacabtagene autoleucel	CARTITUDE-1, phase 1b/2; RRMM; n=97	**ORR 98**%; sCR ~ 83%	Median PFS 34.9 mo median OS 60.7 mo
Ciltacabtagene autoleucel	CARTITUDE-4, phase 3; lenalidomide-refractory RRMM after 1–3 prior lines; cilta-cel vs PVd/DPd	**ORR 84.6%;** ≥CR 73.1% vs 21.8%	30-mo PFS 59.4% vs 25.7% 30-mo OS 76.4% vs 63.8%, OS HR 0.55.

CARTITUDE-1: Third of Patients Progression-Free for ≥5 Years

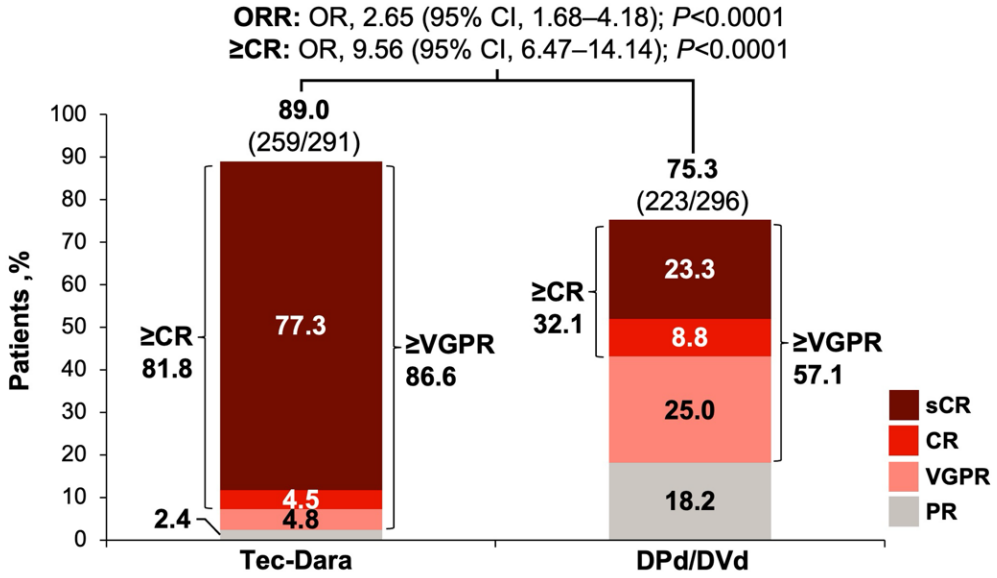


32 of 97 (33%) patients were treatment- and progression-free at ≥5 years

Bispecific antibodies

Agent	Target	Key trial / population	Response rate	Survival / durability
Teclistamab	BCMA	MajesTEC-1, RRMM; n=165	**ORR 63.0**% ≥CR 46.1%	Median DOR 24.0 mo; median PFS 11.4 mo; median OS 22.2 mo
Elranatamab	BCMA	MagnetisMM-3, RRMM; n=123	**ORR 61.0**% ≥CR 37.4%	30-mo DOR 61.0%; median PFS 17.2 mo; median OS 24.6 mo.
Linvoseltamab	BCMA	LINKER-MM1, RRMM; n=117	**ORR 71**% ≥CR 52%	Median DOR 29.4 mos; median PFS NR; median OS 31.4 mos
Talquetamab	GPRC5D	MonumenTAL-1; RRMM; 0.4 mg/kg weekly n=143, 0.8 mg/kg q2wk n≈145	**ORR 74%** q wk / 72% q2wk; ≥CR 34% / 39%	Median PFS 7.5 mo q wk / 14.2 mo q2wk; median OS NR; 12-mo OS 76% / 77%.

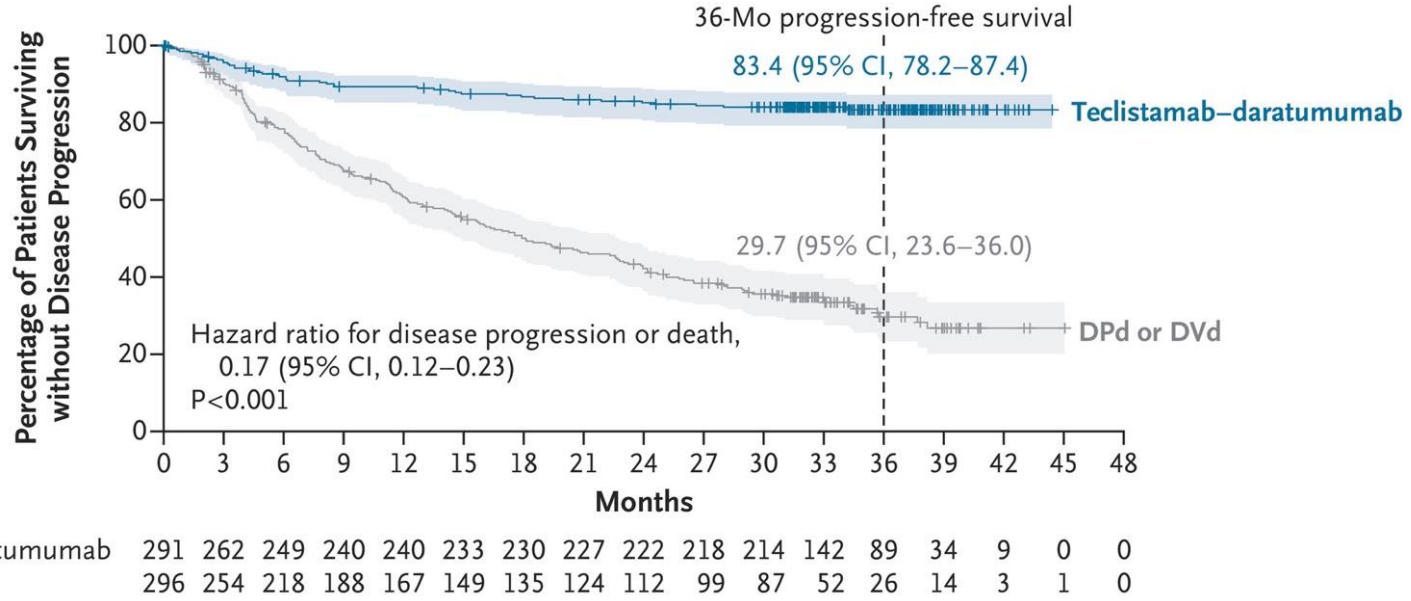
Teclistamab + Daratumumab



	Tec-Dara (n=259)	DPd/DVd (n=223)
Median (range) time to first response, months	1.2 (0.9–25.0)	1.2 (0.7–6.3)
Median (range) time to first ≥CR, months	6.9 (1.0–34.5)	6.9 (1.5–18.8)
Median (95% CI) DOR, months	NE (NE–NE)	23.5 (19.8–29.9)
36-month DOR, % (95% CI)	88.5 (83.7–92.0)	36.4 (28.9–43.9)

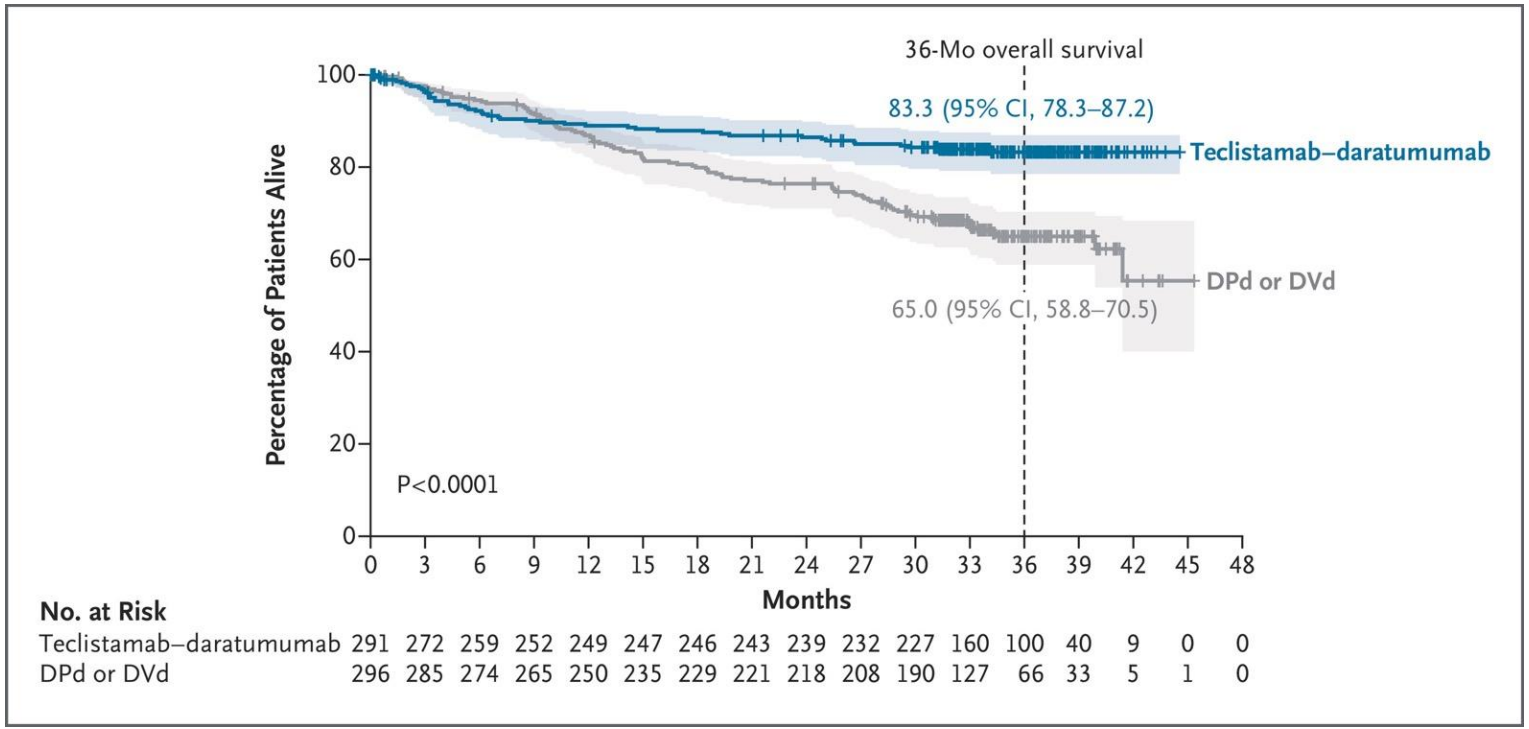
Costa et al, N Engl J Med 2026;394:739-752, Mateos et al, ASH 2025

Teclistamab + Daratumumab - PFS



Costa et al, N Engl J Med 2026

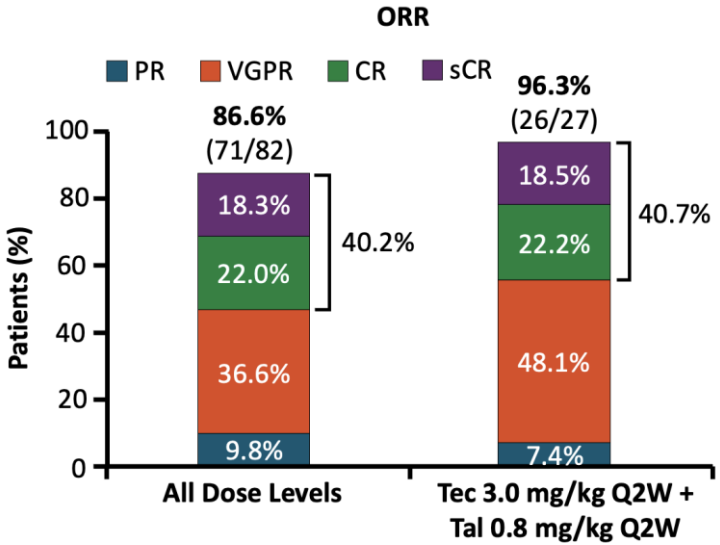
Teclistamab + Daratumumab – Overall survival



Costa et al, N Engl J Med 2026

RedirectTT-1: Teclistamab + Talquetamab

- Open-label, phase Ib/II dose escalation and expansion trial of teclistamab plus talquetamab in patients with R/R MM with previous exposure to a PI, IMiD, and anti-CD38 mAb and refractory to last line of therapy

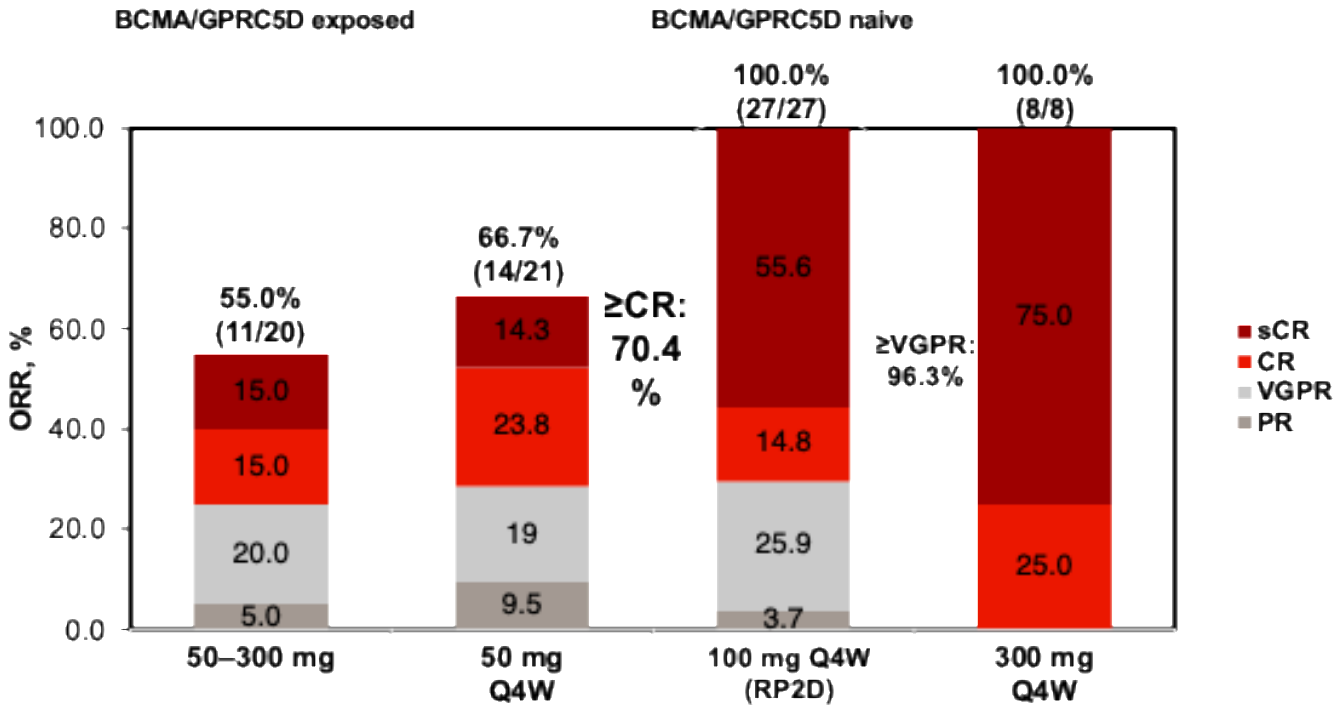


	All Dose Levels (N = 93)	RP2R* (N = 34)
Median f/u, mo (range)	13.4 (0.3-25.6)	8.1 (0.7-15.0)
Median DoR, mo (95% CI)	NE (NE-NE)	NE (NE-NE)
Median time to first response, mo (range)	1.97 (0-7.7)	1.48 (0-4.0)
Median time to best response, mo (range)	3.98 (1.1-15.7)	3.22 (1.4-10.7)
Median PFS, mo (95% CI)	20.9 (13.0-NE)	NE (9.9-NE)
9-mo PFS, % (95% CI)	70.1 (58.0-79.4)	77.1 (50.8-90.5)

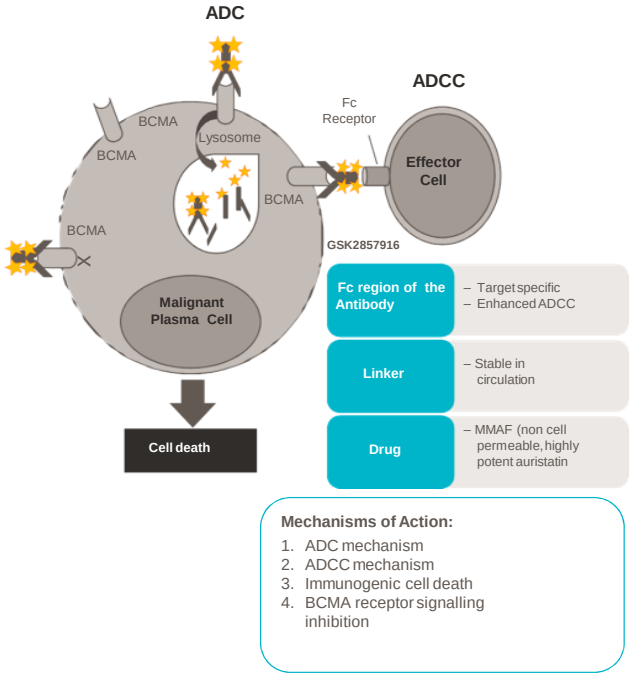
*Teclistamab 3.0 mg/kg Q2W + talquetamab 0.8 mg/kg Q2W.

Mateos. EAH 2023. Abstr S190. NCT04586426.

JNJ-5322 Trispecific Antibody

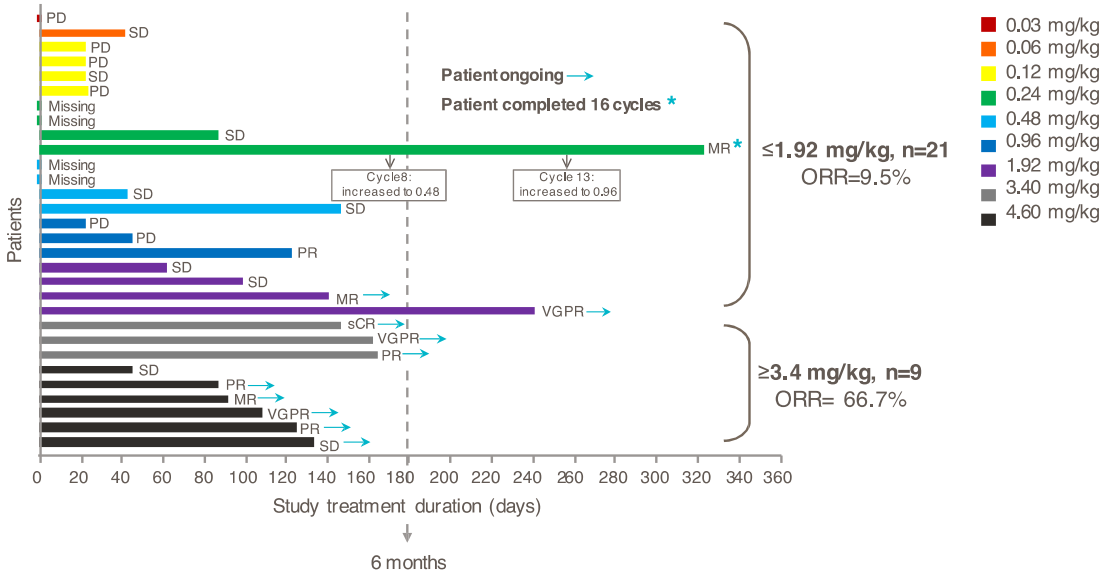


BCMA targeted Antibody-Drug Conjugate: Belantamab

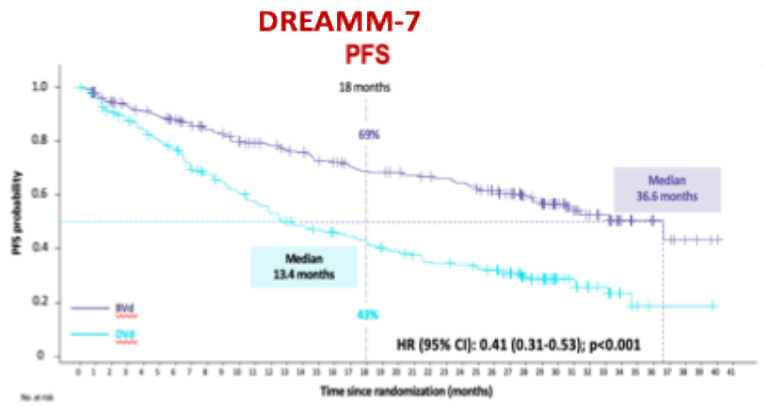


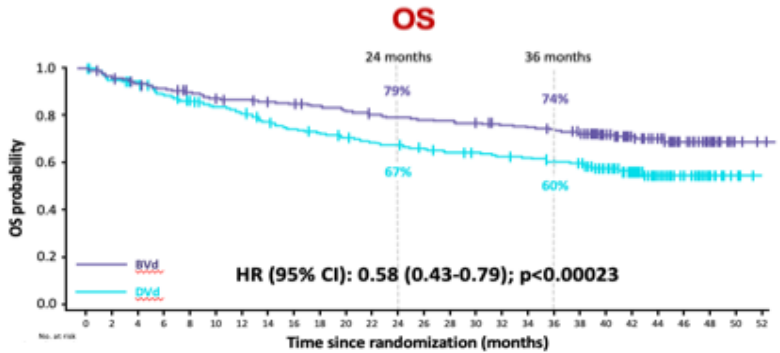
Mechanisms of Action:

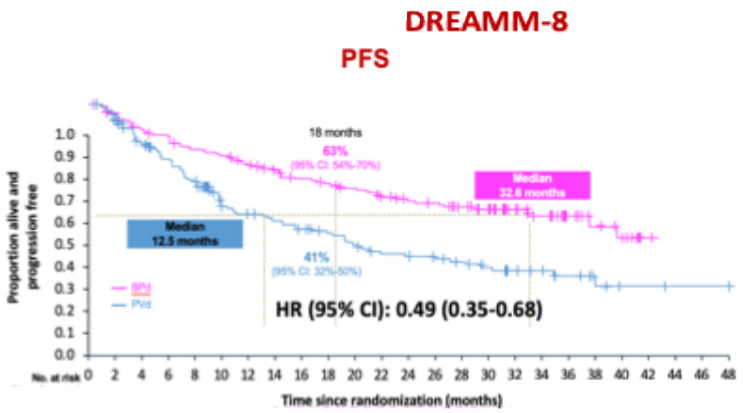
1. ADC mechanism
2. ADCC mechanism
3. Immunogenic cell death
4. BCMA receptor signalling inhibition

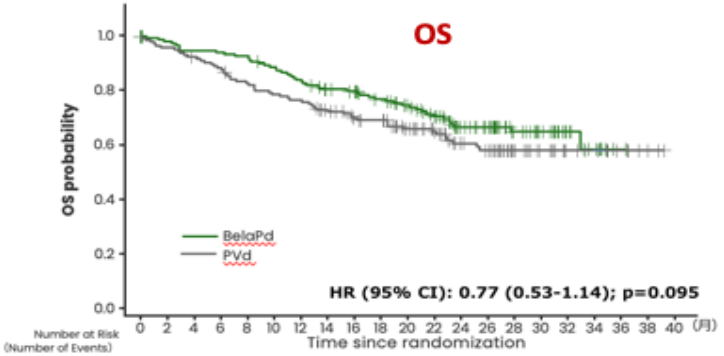


Targeting BCMA:Belantamab combinations



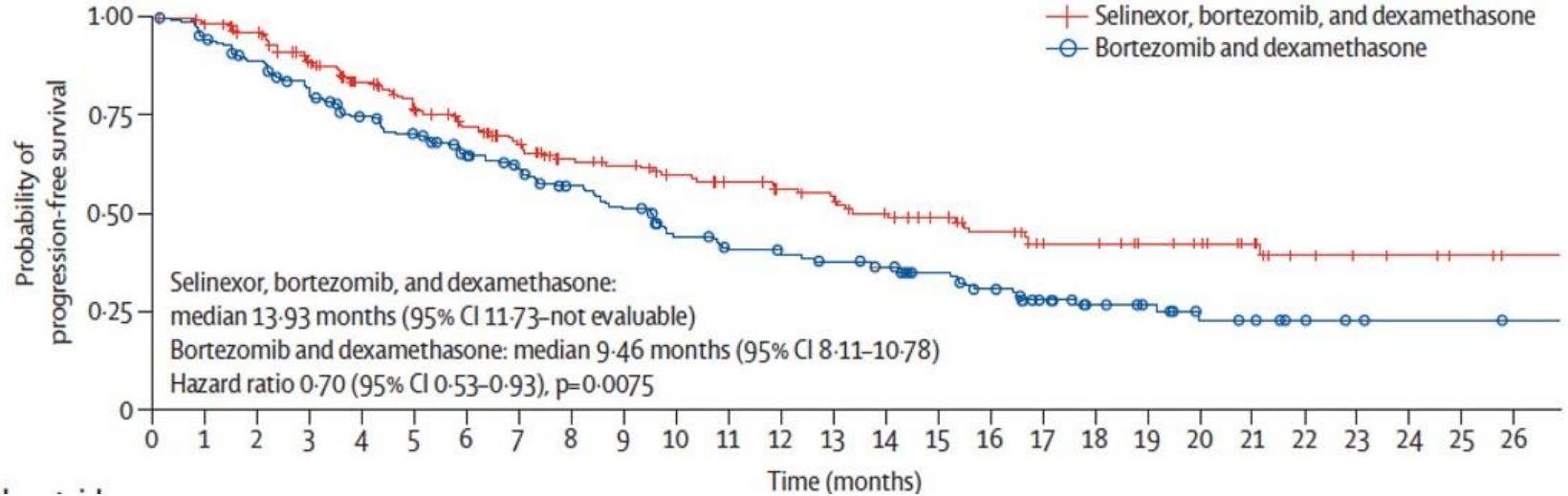






Hungria V, et al. *New Engl J Med*. 2024;391:393-407; Dimopoulos et al. EHA 2025. #PF728

BOSTON Trial: Selinexor bortezomib Dex



Groscki et al, Lancet, 2020

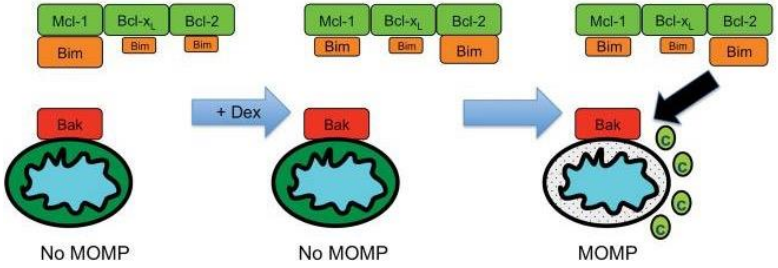
Venetoclax and t(11;14) Multiple Myeloma

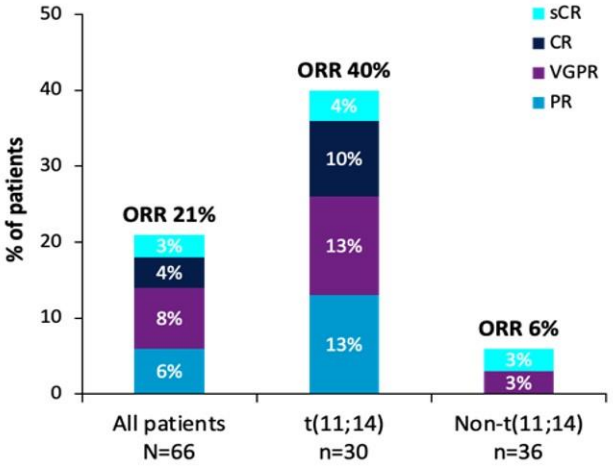
Primary abnormalities

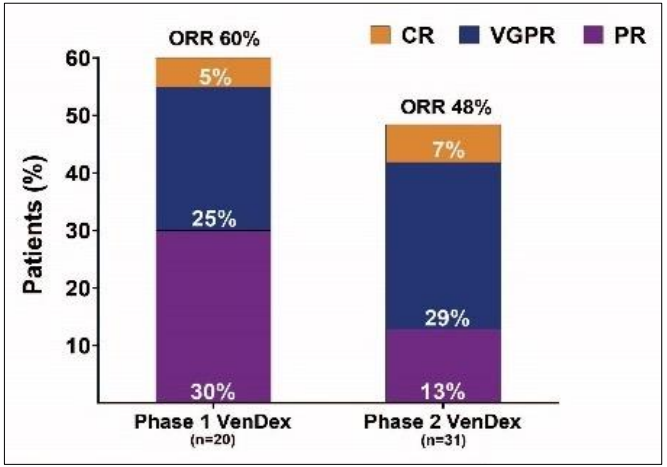
Trisomies (~45%)
Odd-numbered chromosomes: 3, 5, 7, 9, 11, 15, 19, and 21

IgH translocations (~55%)
Translocations involving the IgH gene locus at 14q32

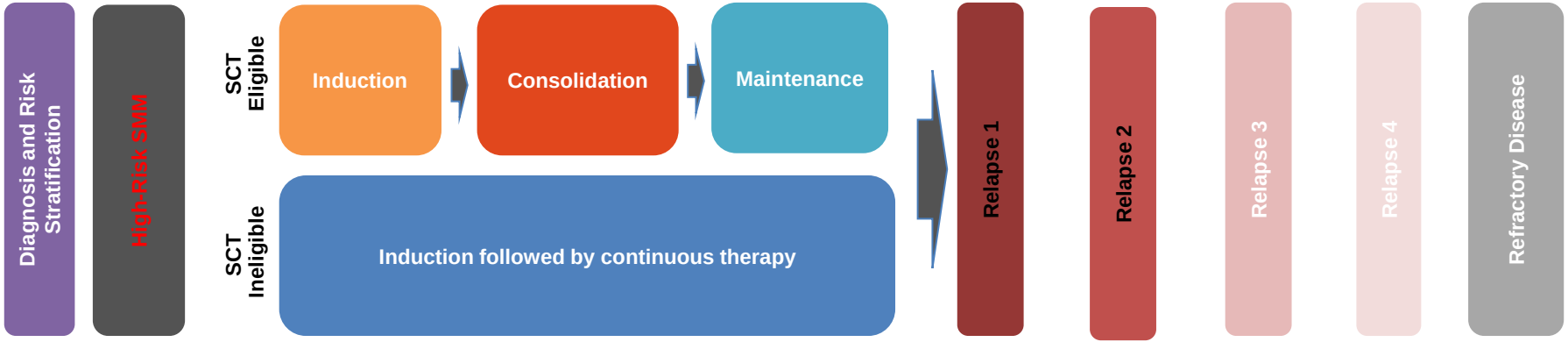
Translocation;locus;gene
t(4;14);4p16;*FGFR3–MMSET*
t(14;16);16q23;*MAF*
t(14;20);20q12;*MAFB*
t(8;14);8q24;*MAFA*
t(11;14);11q13;*CCND1*
t(6;14);6p21;*CCND3*

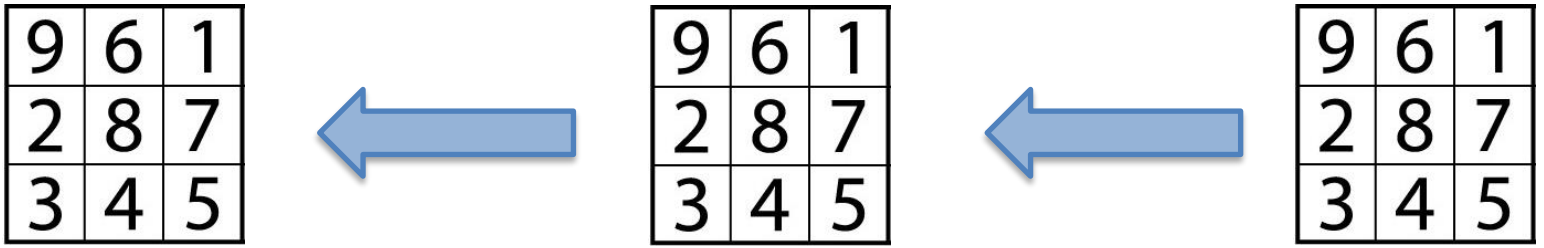




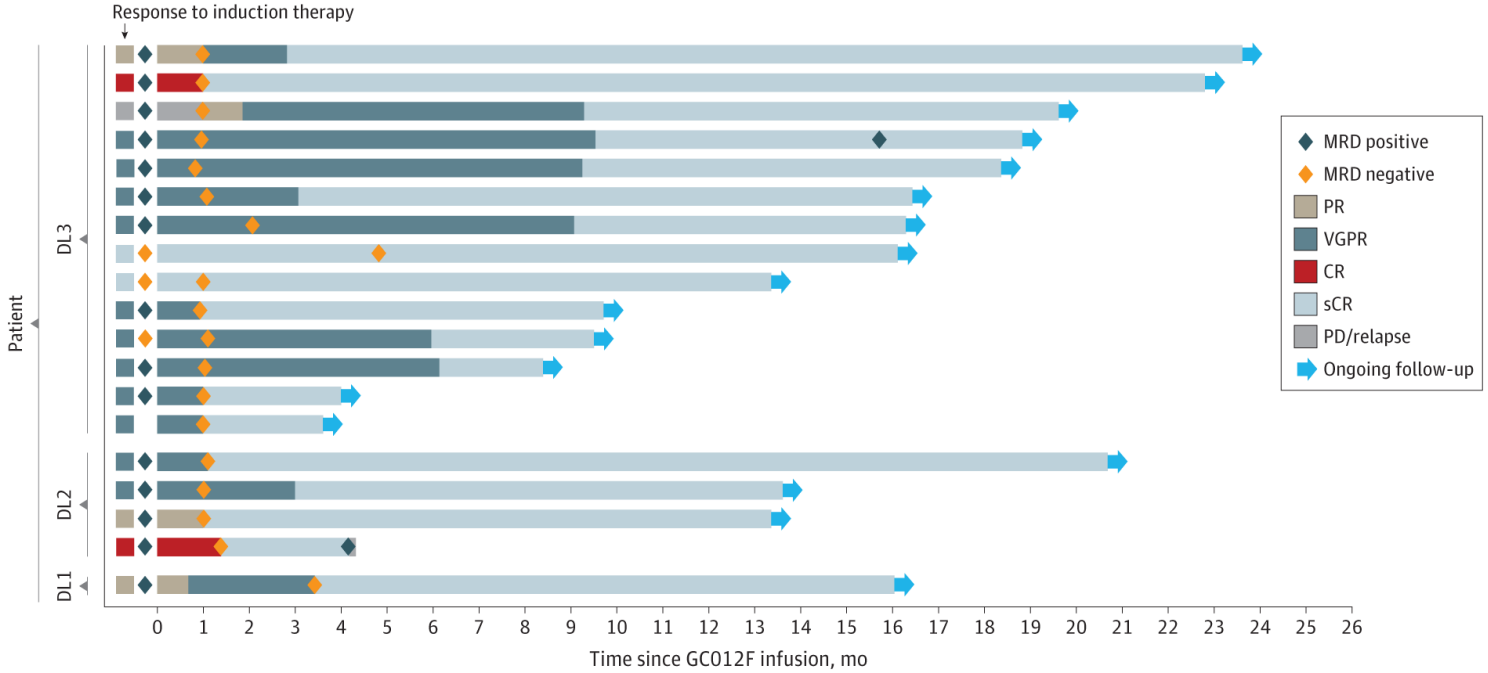


Myeloma Treatment Paradigm



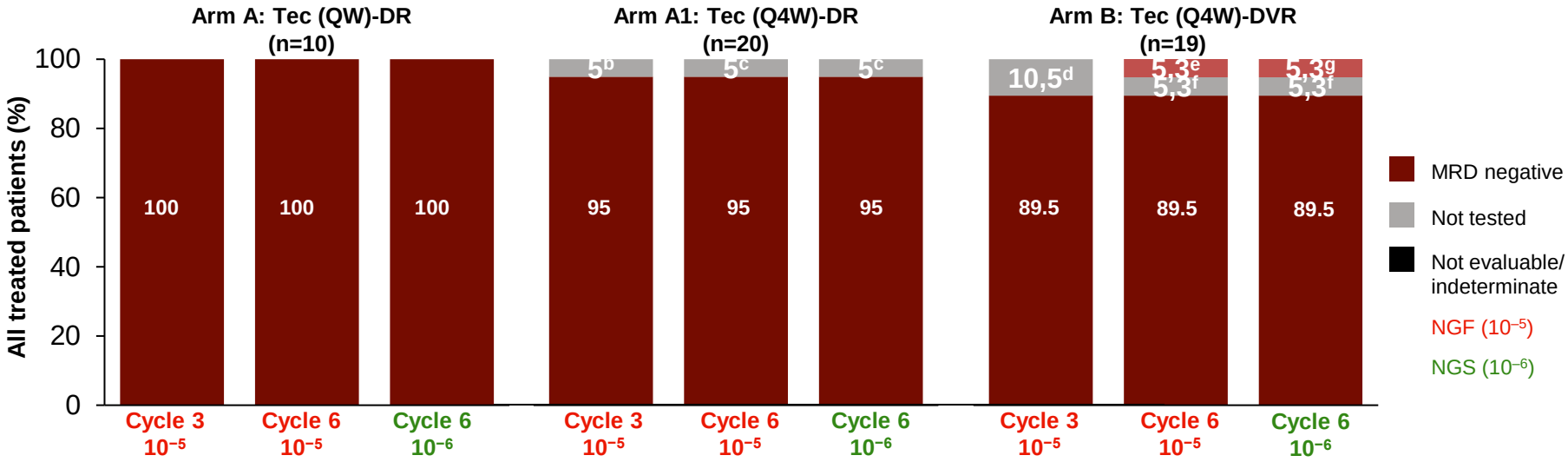


What about CART for newly diagnosed?



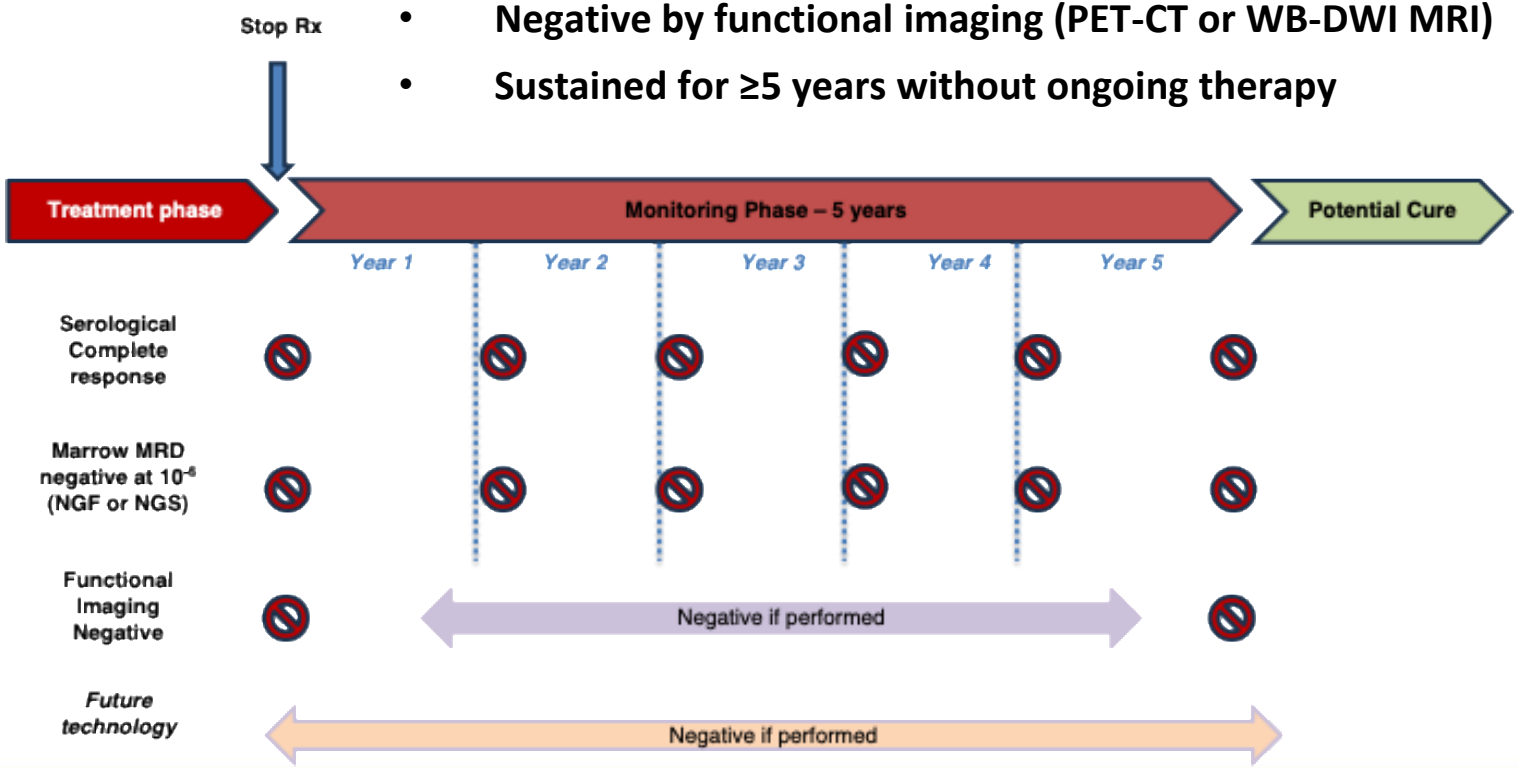
Adding bispecific for newly diagnosed MM

- Efficacy analysis set: all patients who received ≥1 dose of study treatment



CURE?

- MRD at 10^{-6} by NGS
- Negative by functional imaging (PET-CT or WB-DWI MRI)
- Sustained for ≥5 years without ongoing therapy



Future Directions

- Bispecific antibody combinations with PI, IMiDs and anti-CD38 MoABs are being explored
- Tri-specific antibodies appear to have excellent efficacy
- Dual targeted and next generation CARTS with better efficacy and safety are in trials
- CELMODs (Iberdomide and mezigdomide) are in phase 3 trials – positive results reported
- Small molecule drugs include protein degraders, bcl2 inhibitors, MMSET inhibitors
- Increasingly – the field is moving towards limited duration

5	3			7				
6			1	9	5			
	9	8					6	
8				6				3
4			8		3			1
7				2				6
	6					2	8	
			4	1	9			5
				8			7	9

SUDOKU PUZZLE

5	3	4	2	7	6	9	1	8
6	2	8	1	9	5	3	4	7
1	7	9	3	4	8	5	6	2
8	5	2	7	6	1	4	9	3
4	9	6	8	5	3	7	2	1
7	1	3	9	2	4	8	5	6
9	6	1	5	3	7	2	8	4
2	8	7	4	1	9	6	3	5
3	4	5	6	8	2	1	7	9

SUDOKU SOLVED

MAYO CLINIC

Thank you

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