oncology exchange
fall 2024

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cencora

CELL THERAPY IN MYELOMA—ASCT, BISPECIFICS AND CAR-T: WHERE WE'VE BEEN AND WHERE WE'RE GOING

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DISCLOSURE

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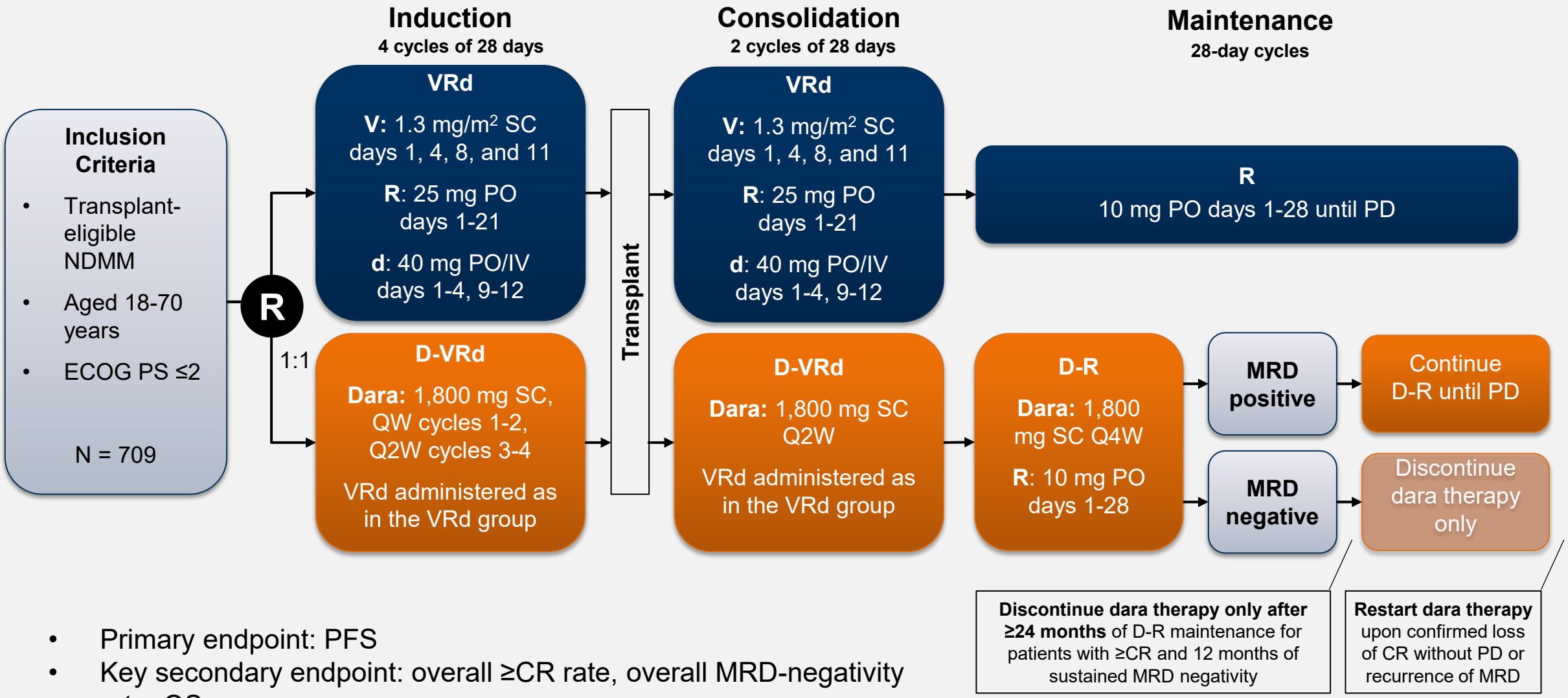
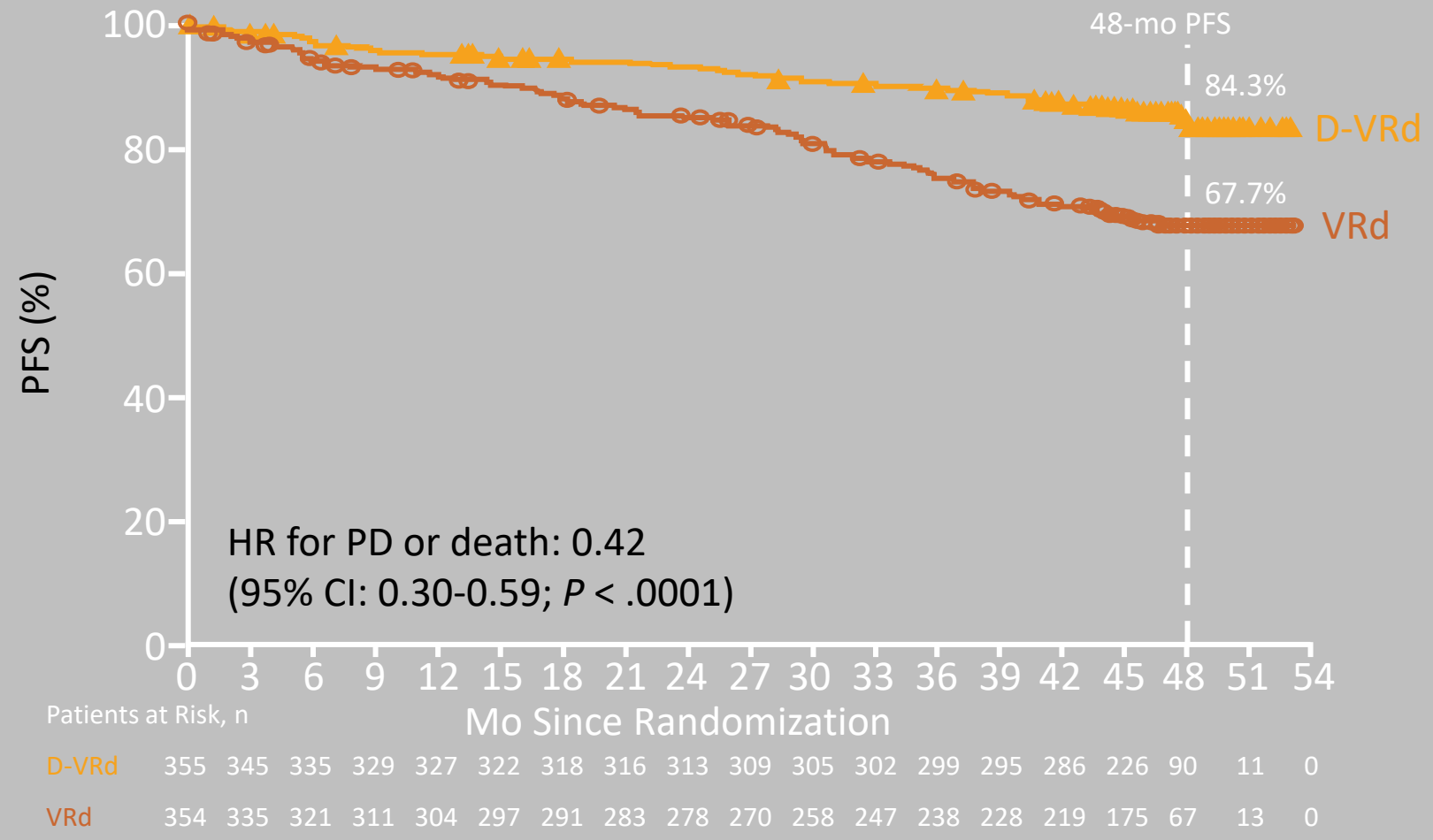
PERSEUS: PHASE 3 COMPARISON OF DARA+VRD VERSUS VRD INDUCTION IN ASCT-ELIGIBLE MM



- Primary endpoint: PFS
- Key secondary endpoint: overall ≥CR rate, overall MRD-negativity rate, OS

???

PERSEUS PRIMARY ANALYSIS: PFS (PRIMARY ENDPOINT)

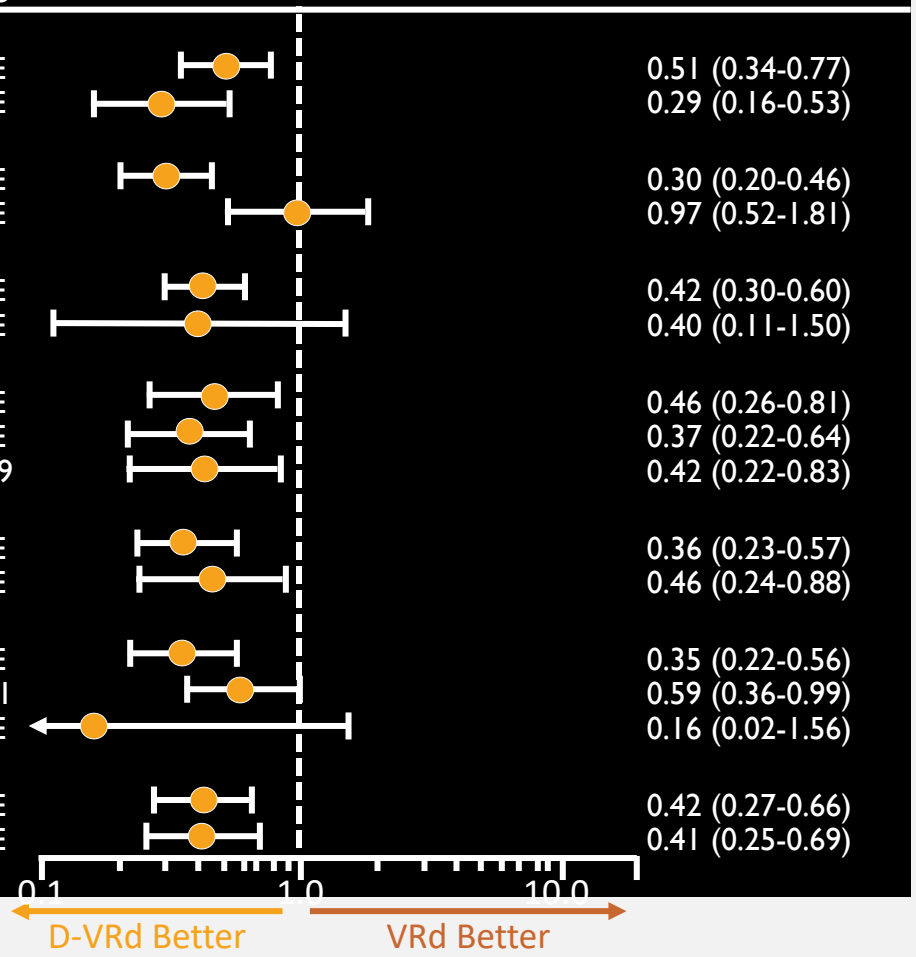


Sonneveld. ASH 2023. Abstr LBA-1. Sonneveld. NEJM. 2023;[Epub].

PERSEUS PRIMARY ANALYSIS: PFS
SUBGROUP ANALYSIS

PD or Death | Median PFS

Subgroup	D-VRd n/N	VRd n/N	D-VRd mo	VRd mo	Hazard Ratio for PD or Death (95% CI)
Sex					
▪ Male	36/211	61/205	NE	NE	0.51 (0.34-0.77)
▪ Female	14/144	42/149	NE	NE	0.29 (0.16-0.53)
Age					
▪ <65 yr	30/261	84/267	NE	NE	0.30 (0.20-0.46)
▪ ≥65 yr	20/94	19/87	NE	NE	0.97 (0.52-1.81)
Race					
▪ White	47/330	95/323	NE	NE	0.42 (0.30-0.60)
▪ Other	3/25	8/31	NE	NE	0.40 (0.11-1.50)
ISS disease stage					
▪ I	18/186	35/178	NE	NE	0.46 (0.26-0.81)
▪ II	19/114	43/125	NE	NE	0.37 (0.22-0.64)
▪ III	13/55	25/50	NE	41.9	0.42 (0.22-0.83)
Type of multiple myeloma					
▪ IgG	28/204	58/185	NE	NE	0.36 (0.23-0.57)
▪ Non-IgG	13/78	31/96	NE	NE	0.46 (0.24-0.88)
Cytogenetic risk					
▪ Standard	25/264	62/266	NE	NE	0.35 (0.22-0.56)
▪ High	24/76	38/78	NE	44.1	0.59 (0.36-0.99)
▪ Indeterminate	1/15	3/10	NE	NE	0.16 (0.02-1.56)
ECOG performance-status score	28/2211	60/230	NE	NE	0.42 (0.27-0.66)
▪ 0	22/134	43/124	NE	NE	0.41 (0.25-0.69)
▪ ≥1					



Sonneveld. ASH 2023. Abstr LBA-1. Sonneveld. NEJM. 2023;[Epub].

PERSEUS PRIMARY ANALYSIS: KEY SECONDARY ENDPOINTS

Efficacy Outcome	D-VRd (n = 355)	VRd (n = 354)	OR (95% CI)	*P* Value
≥CR, %	87.9	70.1	3.13 (2.11-4.65)	<.001
▪ sCR	69.3	44.6		
▪ CR	18.6	25.4		
MRD negativity, %				
10^{-5}	75.2	47.5	3.40 (2.47-4.69)	<.0001
10^{-6}	65.1	32.2	3.97 (2.90-5.43)	<.0001
Sustained MRD negativity (10^{-5}) ≥12 mo, %	64.8	29.7	4.42 (3.22-6.08)	<.0001

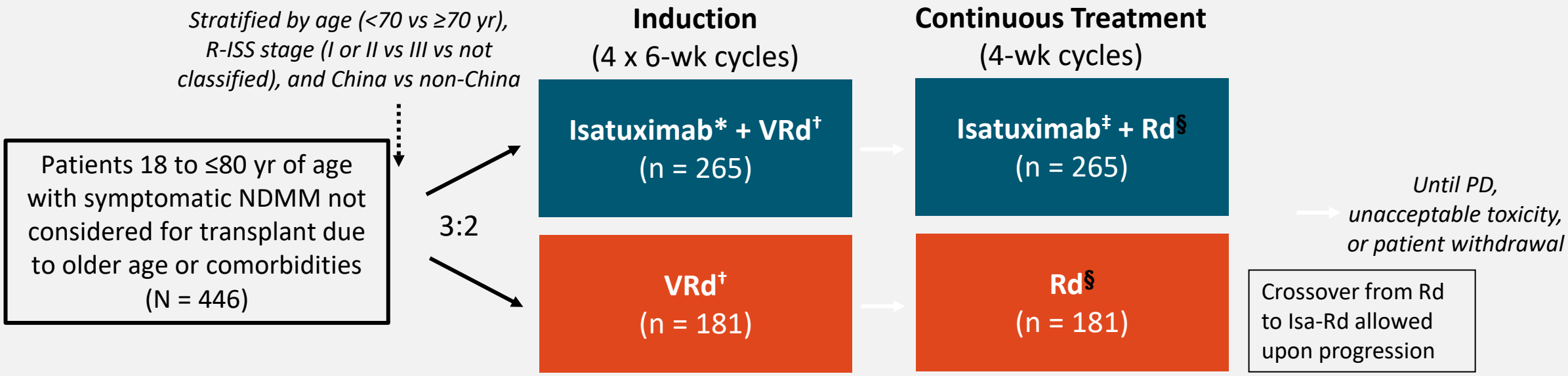
Efficacy Outcome	D-VRd (n = 355)	VRD (n = 354)	Difference Between Arms
MRD negativity (10^{-5}) over time, %			
Post consolidation	57.5	32.5	25.0
Overall	75.2	47.5	27.7
MRD negativity (10^{-6}) over time, %			
▪ Post consolidation	34.4	16.1	18.3
▪ Overall	65.1	32.2	32.9

- Improvements in ≥CR rates with D-VRd vs VRd observed across all subgroups
- 64% of patients in D-VRd arm + D-R maintenance discontinued D after reaching sustained MRD negativity per protocol
- OS data immature
  - Current mortality rate with D-VRd vs VRd: 9.6% vs 12.4% (HR: 0.73)

Sonneveld. ASH 2023. Abstr LBA-1. Sonneveld. NEJM. 2023;[Epub].

IMROZ: STUDY DESIGN

- International, randomized, open-label phase III trial



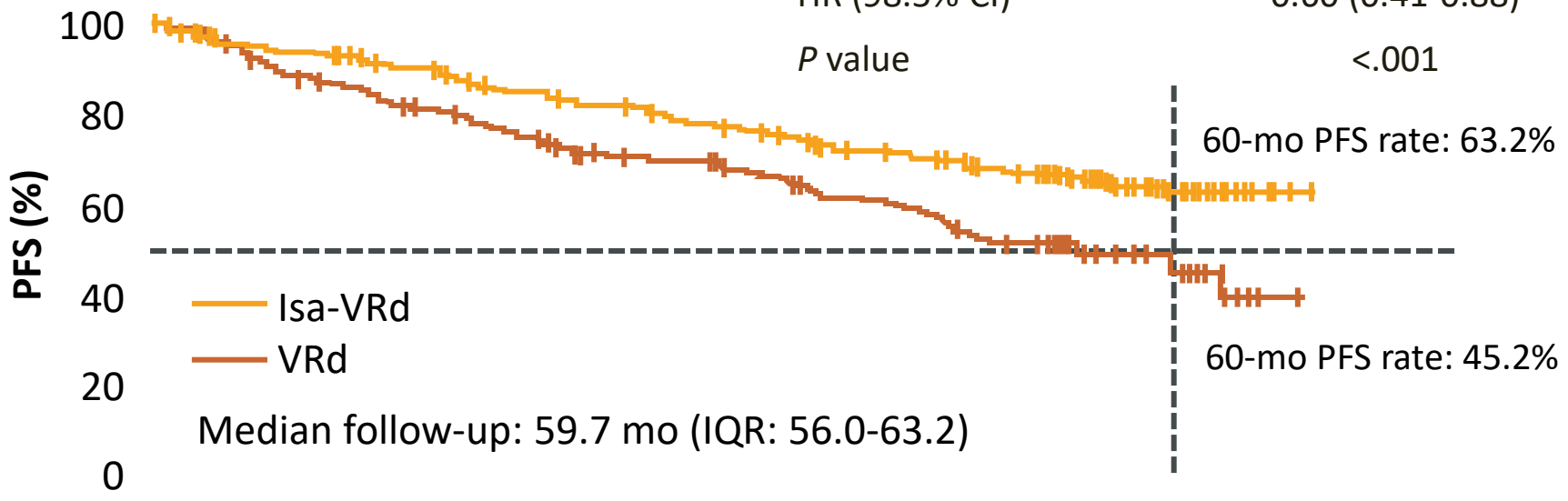
*Isa IV (C1 only) 10 mg/kg Q1W; Isa IV (C2-4) 10 mg/kg Q2W. †V: SC 1.3 mg/m^2 on D1,4,8,11,22,25,29,32; R: PO 25 mg on D1-14 and 22-35; d: IV/PO 20 mg on D1,2,4,5,8,9,11,12,15,22,23,25,26,29,30,32,33. ‡Isa IV (C5-17) 10 mg/kg Q2W; Isa IV (C18+) 10 mg/kg monthly. §R: PO 25 mg on D1-21; d: IV/PO 20 mg on Q1W.

- **Primary endpoints:** PFS
- **Secondary endpoints:** CR rate, MRD− CR (NGS 10^{-5}) rate, ≥ VGPR rate, OS

Facon. ASCO 2024. Abstr 7500. Facon. NEJM. 2024;[Epub].

IMROZ: PFS IN ITT POPULATION, INTERIM ANALYSIS

Parameter, n (%)	Isa + VRd (n = 265)	VRd (n = 181)
Median PFS, mo	NR	54.34
HR (98.5% CI)	0.60 (0.41-0.88)	
P value	<.001	



Patients at Risk, n	0	6	12	18	24	30	36	42	48	54	60	66	72
							Mo						
Isa-VRd	265	243	234	217	201	190	177	164	153	104	43	2	0
VRd	181	155	141	121	104	96	89	81	70	51	20	2	0

Facon. ASCO 2024. Abstr 7500. Facon. NEJM. 2024;[Epub].

IMROZ: RESPONSE, MRD NEGATIVITY, OS, AND QOL

Response, %	Isa-VRd (n = 265)	VRd (n = 181)
ORR	91.3	92.3
▪ sCR	10.9	5.5
▪ CR	63.8	58.6
▪ VGPR	14.3	18.8
▪ PR	2.3	9.4
≥ CR	74.7	64.1
	P = .01	
≥ VGPR	89.1	82.9
▪ OR (95% CI)	1.73 (0.99-3.01)	

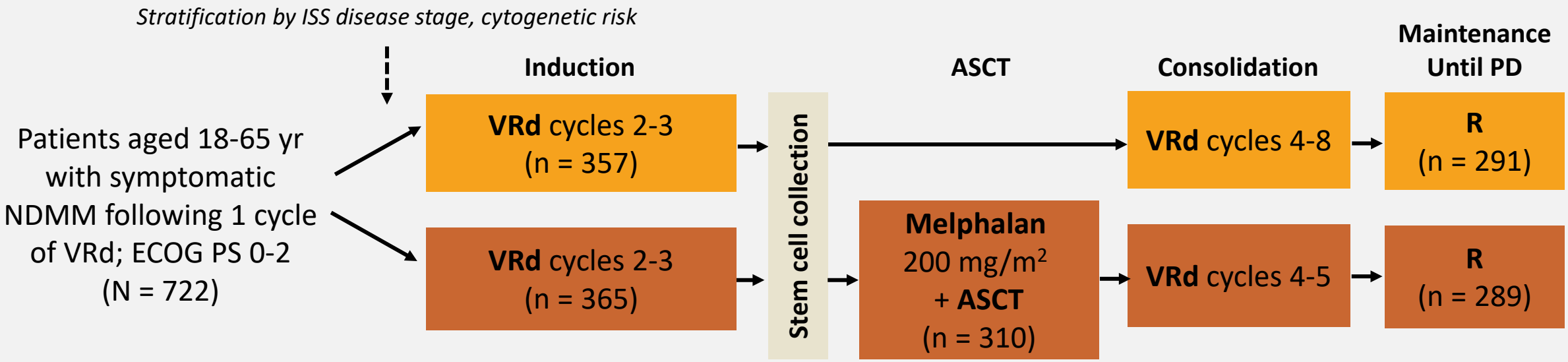
MRD-Negative In Given Patient Population, %	Isa-VRd (n = 265)	VRd (n = 181)
ITT	58.1	43.6
OR (95% CI)	1.79 (1.22-2.63)	
CR	55.5	40.9
OR (95% CI)	1.80 (1.23-2.65)	
Sustained ≥12 mo	46.8	24.3
OR (95% CI)	2.73 (1.80-4.14)	
Median time to MRD-, mo (95% CI)	14.72 (11.53-24.08)	32.79 (17.51-45.11)

- OS data immature at 5-yr analysis
  - 60-mo OS rate: 72.3% vs 66.3% for Isa-VRd vs VRd, respectively; HR: 0.78 (99.97% CI: 0.41-1.48)
- QoL similar between 2 arms

Facon. ASCO 2024. Abstr 7500. Facon. NEJM. 2024;[Epub].

DETERMINATION: STUDY DESIGN

- Multicenter, randomized, open-label phase III trial conducted in 56 sites within the United States

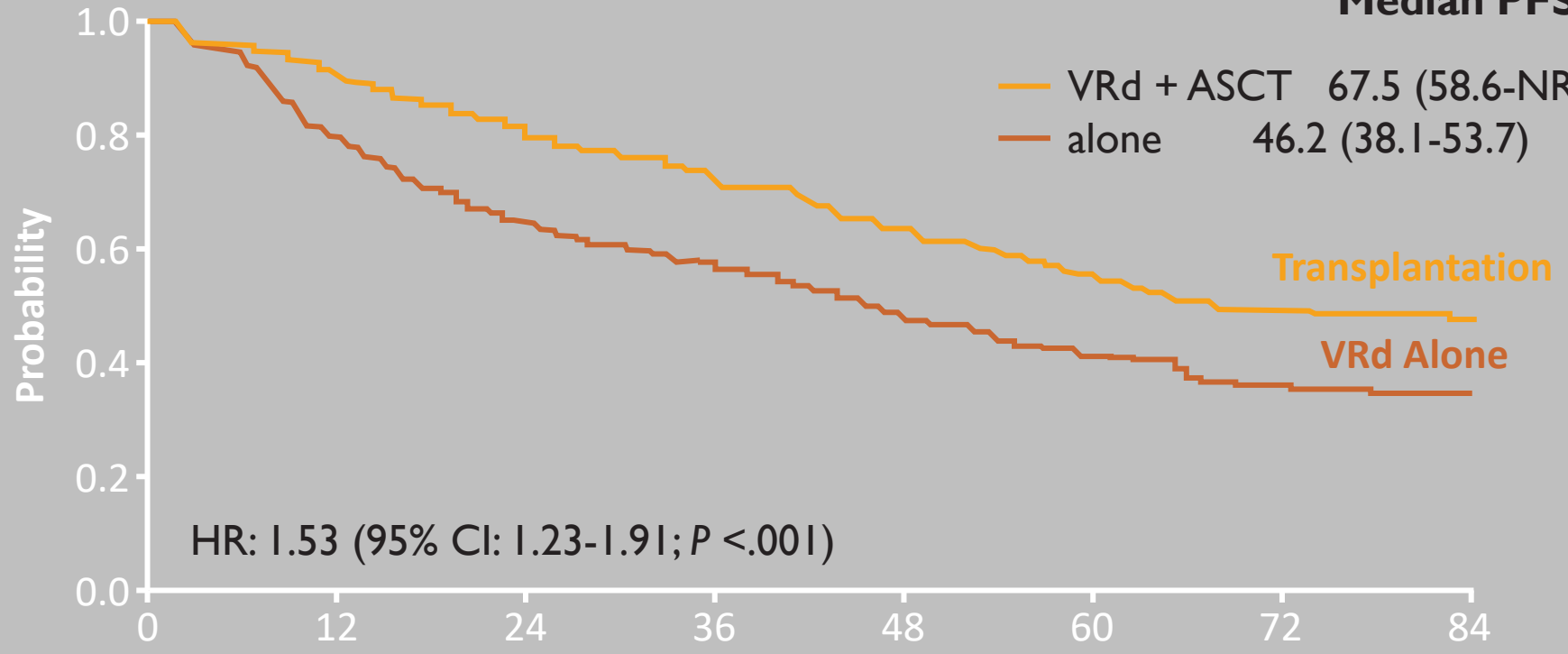


VRd in 21-day cycles: R 25 mg/day PO Days 1-14; V 1.3 mg/m^2 IV/SC Days 1, 4, 8, 11; d 20/10 mg PO Days 1, 2, 4, 5, 8, 9, 11, 12.
R maintenance 10 mg/day during Mo 1-3, 15 mg/day from Mo 4 onward.

- **Primary endpoint:** PFS
- **Key secondary endpoints:** DoR, TTP, OS, QoL, safety

Richardson. ASCO 2022. Abstr LBA4. Richardson. NEJM. 2022;[Epub].

DETERMINATION: PFS (PRIMARY ENDPOINT)



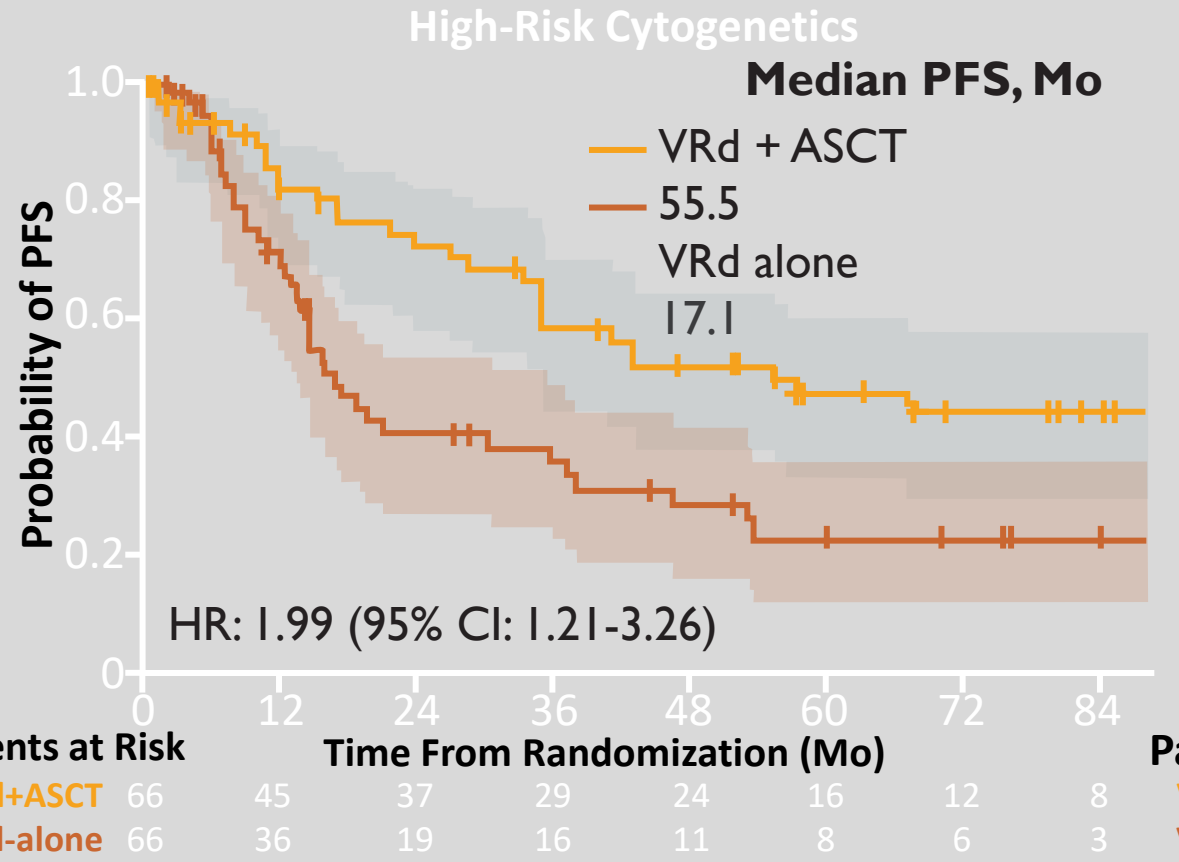
No. at Risk

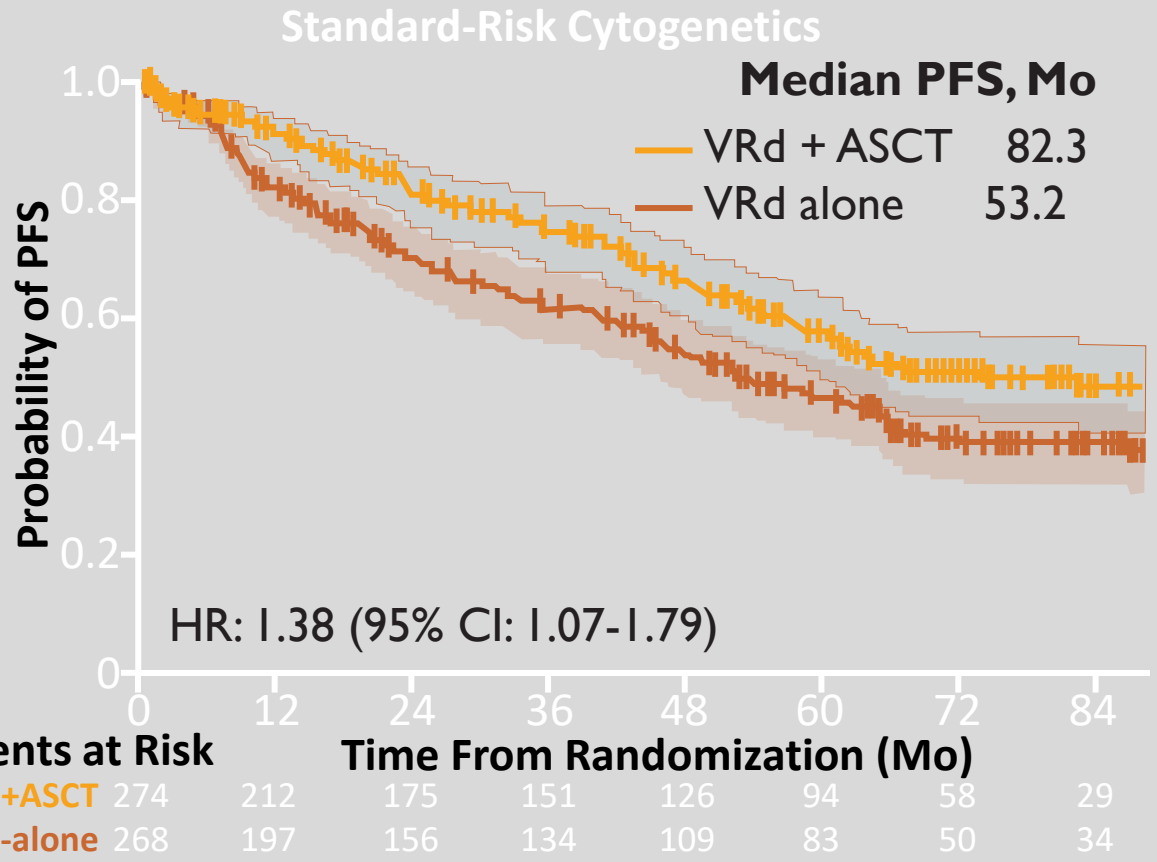
Transplantation	365	276	226	191	160	118	77	42
VRd Alone	357	250	187	160	126	96	60	40

- Median follow-up: 76 mo

Richardson. ASCO 2022. Abstr LBA4. Richardson. NEJM. 2022;[Epub].

DETERMINATION: PFS BY CYTOGENETIC RISK





- Median follow-up: 76 mo

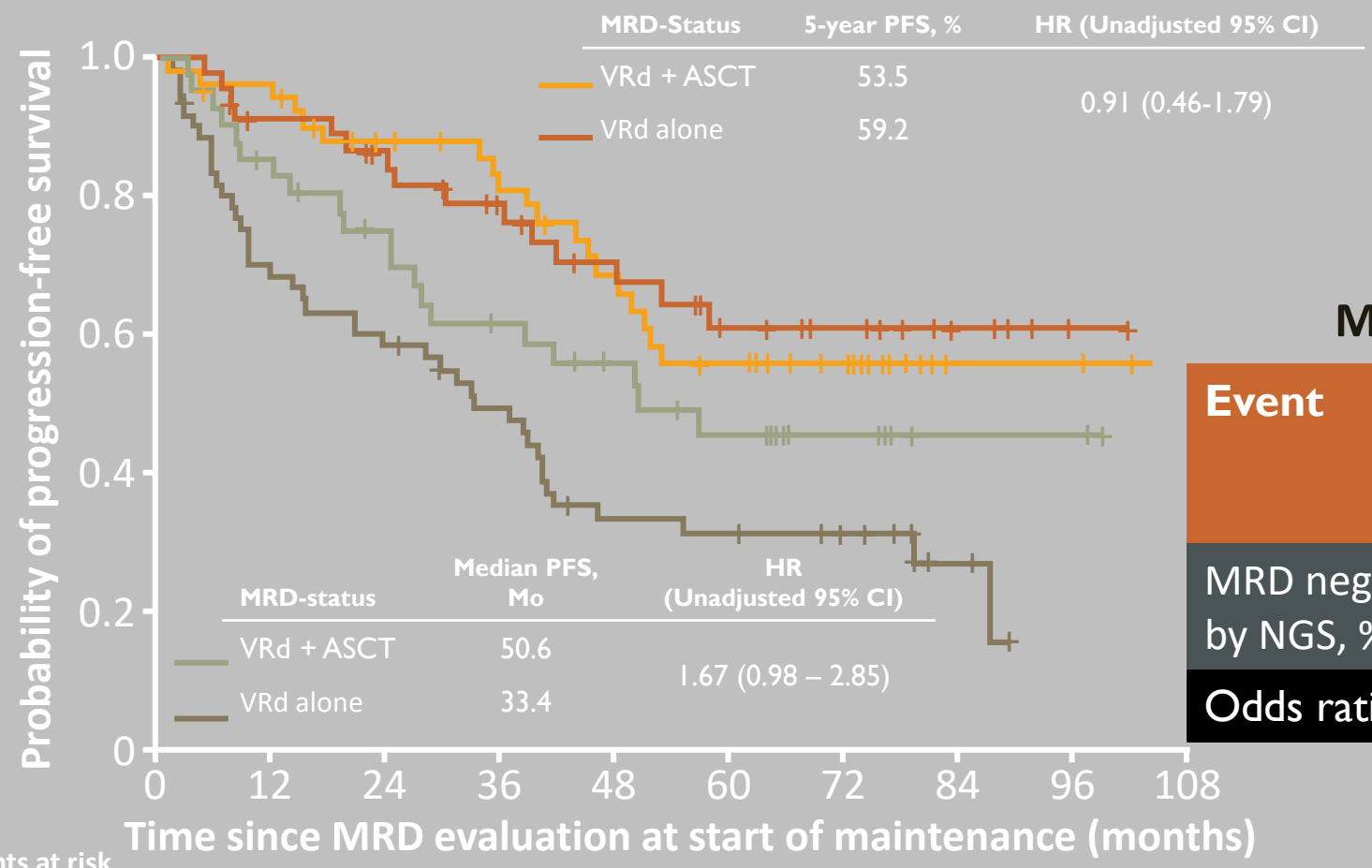
Richardson. ASCO 2022. Abstr LBA4. Richardson. NEJM. 2022;[Epub].

DETERMINATION: PFS IN SUBGROUPS

Subgroup analysis for progression-free survival	No. of events/ total no. of patients		Median, months		HR	(95% CI)
	VRd-alone	VRd-ASCT	VRd-alone	VRd-ASCT		
All patients, ITT analysis	189/357	139/365	46.2	67.5	1.53	(1.23-1.91)
Age						
< 60 years	122/235	100/283	46.2	73.8	1.49	(1.14-1.95)
≥ 60 years	67/122	39/102	46.5	66.5	1.59	(1.05-2.40)
Sex						
Male	107/202	81/215	47.4	66.5	1.50	(1.11-2.02)
Female	82/155	58/150	45.3	82.3	1.54	(1.09-2.17)
Race						
White/Caucasian	150/268	104/272	44.3	67.2	1.67	(1.29-2.15)
Black/African American	24/66	24/66	NR	61.4	1.07	(0.61-1.89)
Other	12/17	5/21	38.1	NR	3.40	(1.00-11.5)
ECOG performance status						
0	75/153	54/164	56.7	67.2	1.32	(0.94-1.85)
1-2	113/204	75/200	37.5	67.5	1.72	(1.28-2.32)
Body mass index						
< 25	49/80	25/81	33.6	NR	2.60	(1.56-4.31)
25 to < 30	71/141	54/127	52.3	64.3	1.24	(0.86-1.80)
≥ 30	69/136	61/157	45.8	64.4	1.41	(0.98-2.02)
Myeloma type						
IgG	108/220	80/200	53.3	67.2	1.25	(0.93-1.67)
IgA	43/72	33/95	46.5	NR	2.31	(1.43-3.74)
Light chain	21/34	16/41	23.3	57.5	2.33	(1.14-4.74)
ISS stage						
I	89/178	62/184	52.0	NR	1.83	(1.32-2.54)
II	69/130	56/134	46.2	62.5	1.38	(0.96-1.96)
III	31/49	21/47	40.3	35.9	1.14	(0.64-2.01)
Lactate dehydrogenase level						
Not elevated (< 225 U/L)	132/260	106/270	47.7	67.2	1.45	(1.12-1.88)
Elevated (≥ 225 U/L)	58/96	31/92	41.1	NR	1.77	(1.09-2.88)
FISH cytogenetics						
High risk	37/66	28/68	17.1	55.5	1.99	(1.21-3.26)
b (4, 14)	18/32	11/28	19.8	56.5	2.72	(1.19-6.24)
Del (17p)	22/38	18/34	16.3	41.3	1.44	(0.79-2.73)
Standard risk	135/268	103/274	53.2	82.3	1.38	(1.07-1.79)
Revised-ISS stage						
I	45/103	39/105	59.1	NR	1.38	(0.90-2.12)
II	109/202	78/211	40.9	67.5	1.63	(1.22-2.19)
III	17/28	11/21	22.2	32.6	0.96	(0.43-2.13)

Richardson. ASCO 2022. Abstr LBA4. Richardson. NEJM. 2022;[Epub].

DETERMINATION: PFS BY MRD AT START OF MAINTENANCE



Patients at risk

VRd + ASCT, MRD-	49	47	37	32	25	19	13	3	3	0
VRd alone, MRD-	43	37	33	28	22	16	11	5	1	0
VRd + ASCT, MRD+	41	32	26	20	15	11	6	2	2	0
VRd alone, MRD+	65	39	32	25	15	14	10	3	0	0

Preliminary Analysis of MRD at Start of Maintenance

Event	VRd Alone (n = 108)	VRd + ASCT (n = 90)
MRD negative (10^{-5}) by NGS, %	39.8	54.4
Odds ratio (95% CI)	0.55 (0.30-1.01)	

Richardson. ASCO 2022. Abstr LBA4. Richardson. NEJM. 2022;[Epub].

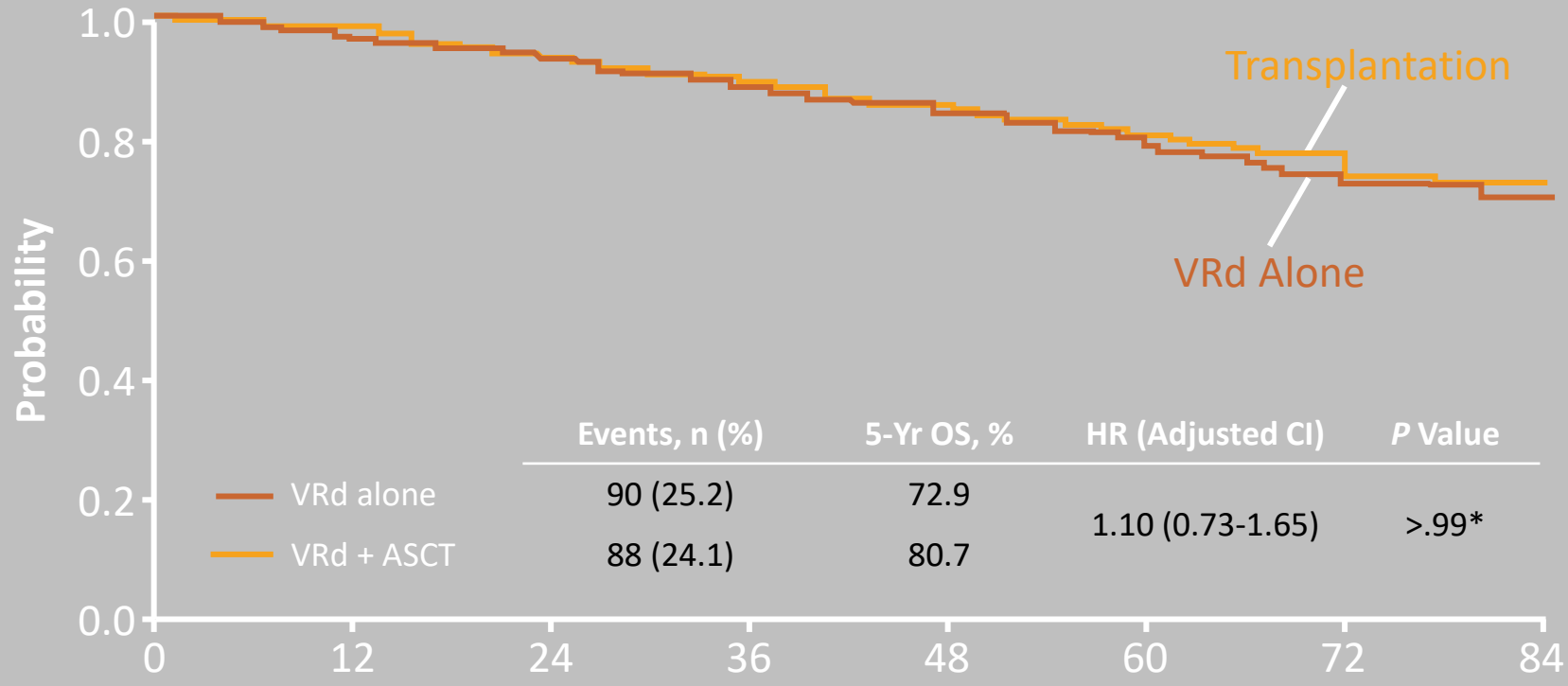
DETERMINATION: RESPONSE AND DURATION OF RESPONSE

Efficacy Endpoint	VRd Alone (n = 357)	VRd + ASCT (n = 365)	HR (95% CI)	*P* Value
Best overall response, %				
▪ ≥ CR	42.0	46.8	--	.99*
▪ ≥ VGPR	79.6	82.7	--	.99*
▪ ≥ PR	95.0	97.5	--	.55*
Median duration of ≥ PR, mo	38.9	56.4	1.45 (1.09-1.93)	.003
5-year duration of ≥ CR, %	52.9	60.6	1.35 (0.83-2.22)	.7

*Calculated with Fisher exact test.

Richardson. ASCO 2022. Abstr LBA4. Richardson. NEJM. 2022;[Epub].

DETERMINATION: OS (KEY SECONDARY ENDPOINT)



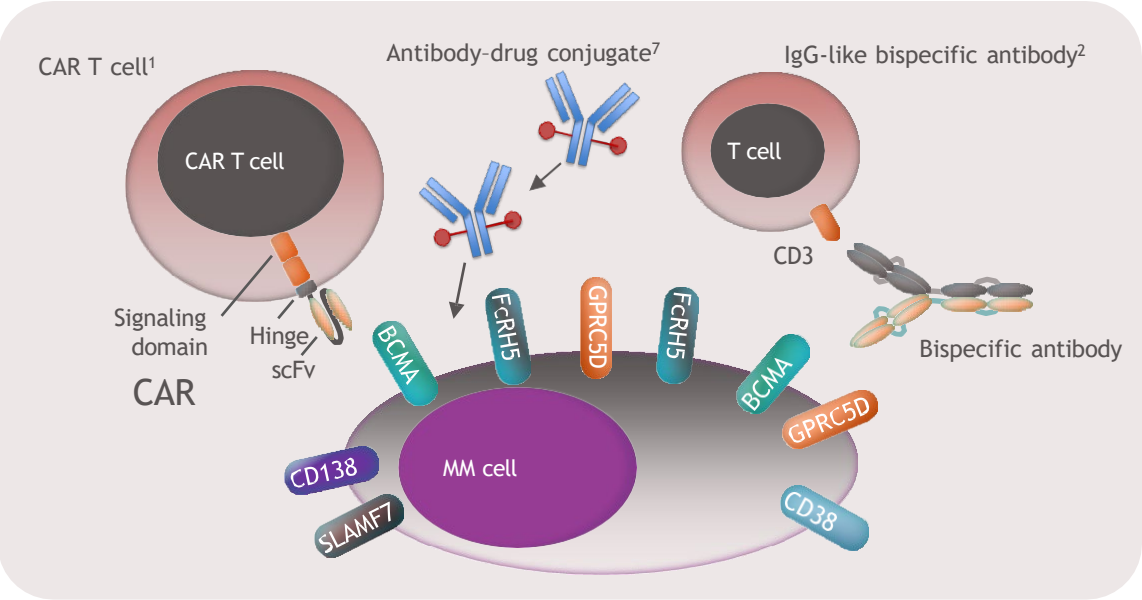
	Events, n (%)	5-Yr OS, %	HR (Adjusted CI)	*P* Value
VRd alone	90 (25.2)	72.9	1.10 (0.73-1.65)	>.99*
VRd + ASCT	88 (24.1)	80.7		

No. at Risk								
Transplantation	365	353	324	300	275	228	165	95
VRd alone	357	332	313	285	258	214	143	88

*CI and *P* value adjusted using Bonferroni correction to control for overall family-wise error rate for secondary outcomes.

Richardson. ASCO 2022. Abstr LBA4. Richardson. NEJM. 2022;[Epub].

CAR-T and BsAbs→New-generation immunotherapies in MM



- ADC:
  Belantamab
  MEDI2228
- Bispecifics:
  AMG701
  Teclistamab,
  talquetamab
  Elranatamab
  REGN5458
  TNB-383B
  CC-93269
  Cevostamab
- CAR T:
  Ide-cel
  Cilta-cel
  p-BCMA-101
  CT053
  ALLO-715

BCMA:[3]
- Selectively overexpressed in plasma cells
- Promotes proliferation and survival of MM cells

GPRC5D:[4,5]
- Highly and selectively expressed in MM
- Distribution is similar to but independent of BCMA

FCRH5:[6]
- High levels of expression on MM cells
- Normally expressed in plasma cells only

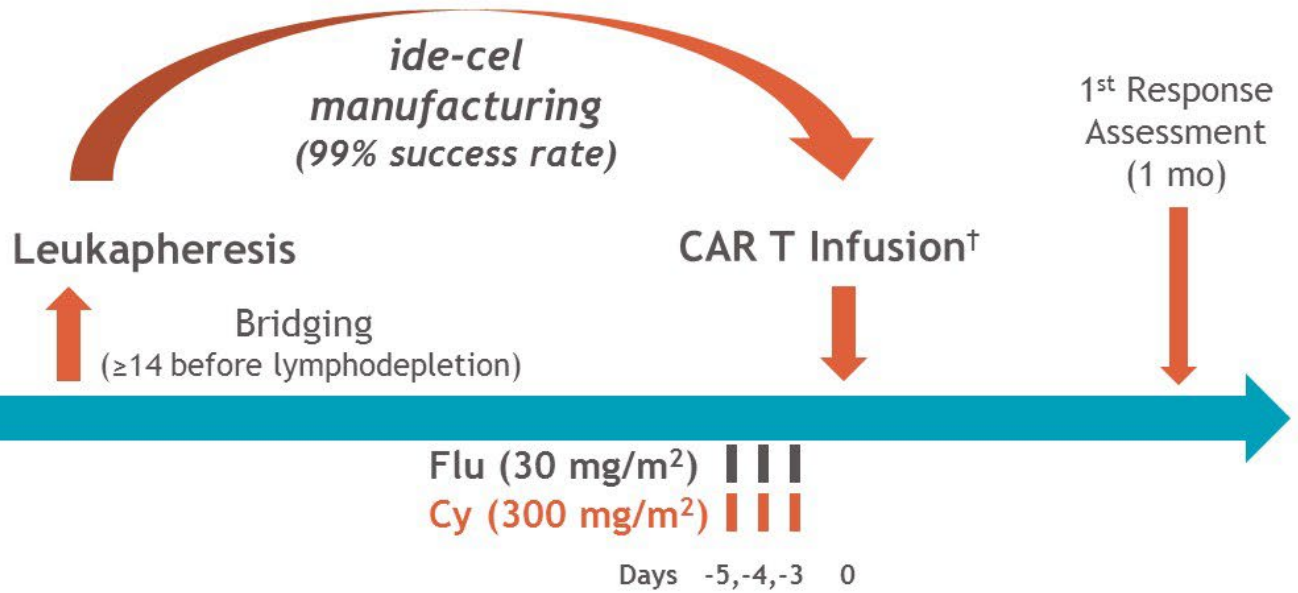
BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; FcRH5, Fc receptor-like 5; GPRC5D, ide-cel, idecabtagene vicleucel; GPRC5D, G-protein coupled receptor family C group 5 member D; Ig, immunoglobulin; scFv, single chain variable fragment.

1. Rodríguez-Lobato LG, et al. Front Oncol. 2020;10:1243. 2. Pillarisetti K, et al. Blood Adv. 2020;4:4538-49. 3. Yu B, et al. J Hematol Oncol. 2020;13:125. 4. Verkleij et al. Blood Advances, 2020;5(8);2195-2215.
5. Smith EL, et al. Sci Transl Med. 2020;11:eaau7746. 6. Li J, et al. Cancer Cell. 2017;31;383-395. 7. Bruins WSC, et al. Front Immunol. 2020;11:1155.
Images adapted from Verkleij CPM, et al. Curr Opin Oncol. 2020;32:664-71 and Bruins WSC, et al. Front Immunol. 2020;11:1155.

Phase II Pivotal KarMMa Study

KarMMa™

- RRMM
- ≥3 prior regimens with ≥2 consecutive cycles each (or best response of PD)
- Previously exposed to:
  - IMiD agent
  - Proteasome inhibitor
  - Anti-CD38 antibody
- Refractory to last prior therapy per IMWG*



Endpoints

- **Primary**: ORR (null hypothesis ≤50%)
- **Secondary**: CRR (key secondary; null hypothesis ≤10%), Safety, DOR, PFS, OS, PK, MRD‡, QOL, HEOR
- **Exploratory**: Immunogenicity, BCMA expression/loss, cytokines, T cell immunophenotype, GEP in BM

Study Status as of Jan 14, 2020

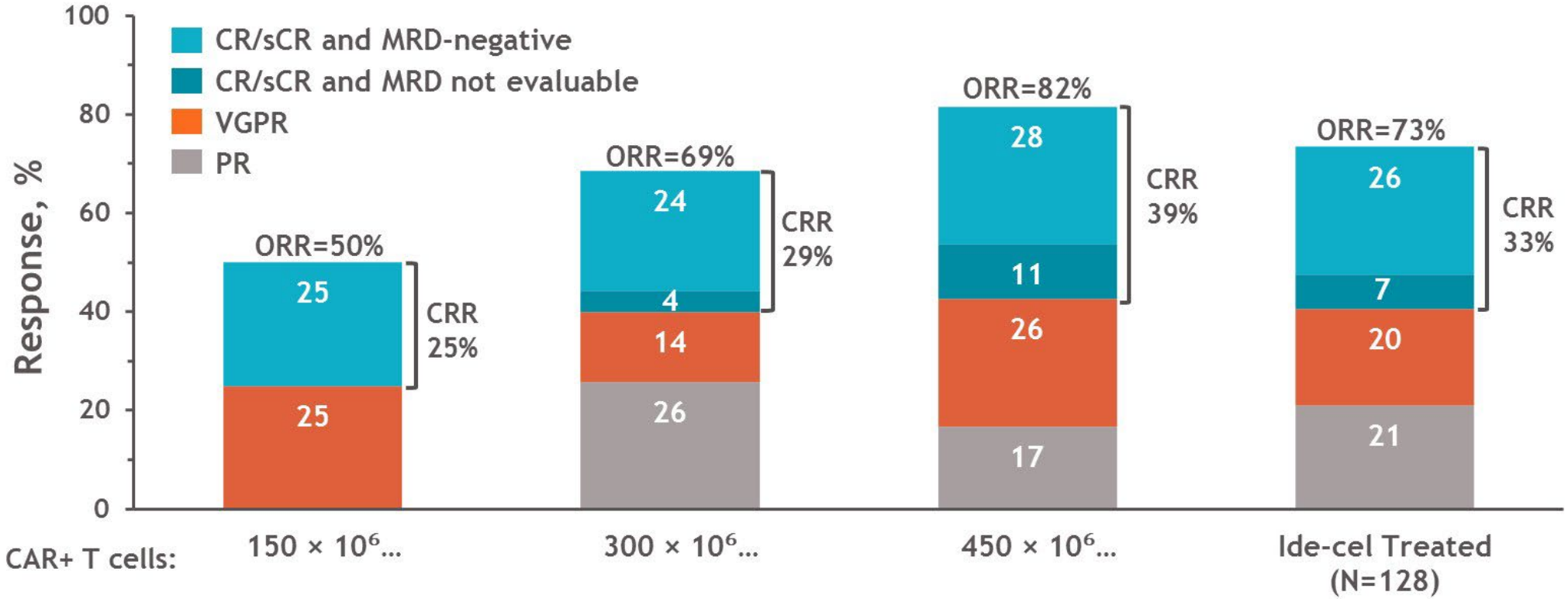
Screened	N=158
Leukapheresed	N=140
Treated (Target Dose CAR+ T cells)	N=128
150×10^6	n=4
300×10^6	n=70
450×10^6	n=54

Median Follow-up (mo)	
150×10^6	18.0
300×10^6	15.8
450×10^6	12.4
Total	13.3

CRR, complete response rate; Cy, cyclophosphamide; DOR, duration of response; Flu, fludarabine; GEP in BM, gene expression profile in bone marrow; HEOR, health economics and outcomes research; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PK, pharmacokinetics; QOL, quality of life.
*Defined as documented disease progression during or within 60 d from last dose of prior antimyeloma regimen. †Patients were required to be hospitalized for 14 d post-infusion. Ide-cel retreatment was allowed at disease progression for best response of at least stable disease. ‡By next-generation sequencing.

EudraCT: 2017-002245-29
ClinicalTrials.gov: NCT03361748

Best Overall Response

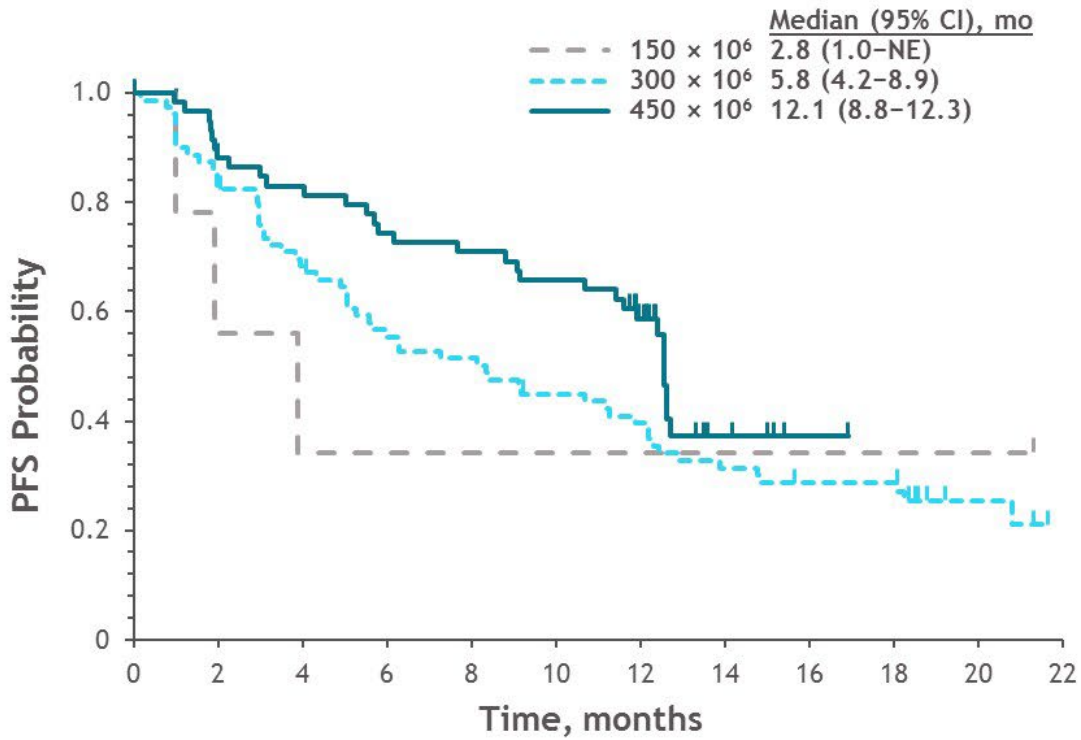


- Primary (ORR >50%) and key secondary (CRR >10%) endpoints met in the ide-cel treated population
  - *ORR of 73% (95% CI, 65.8–81.1; P<0.0001*)*
  - *CRR (CR/sCR) of 33% (95% CI, 24.7–40.9; P<0.0001)*
- Median time to first response of 1.0 mo (range, 0.5–8.8); median time to CR of 2.8 mo (range, 1.0–11.8)
- Median follow-up of 13.3 mo across target dose levels

Data cutoff: 14 Jan 2020. MRD-negative defined as $<10^{-5}$ nucleated cells by next generation sequencing. Only MRD values within 3 mo of achieving CR/sCR until progression/death (exclusive) were considered.
Values may not add up due to rounding.
CR/sCR, complete response/stringent CR; CRR, CR rate; MRD, minimal residual disease; ORR, overall response rate (≥PR); PR, partial response; VGPR, very good PR. **P* value at the primary data cutoff with same ORR and 95% CI.

Progression-Free Survival

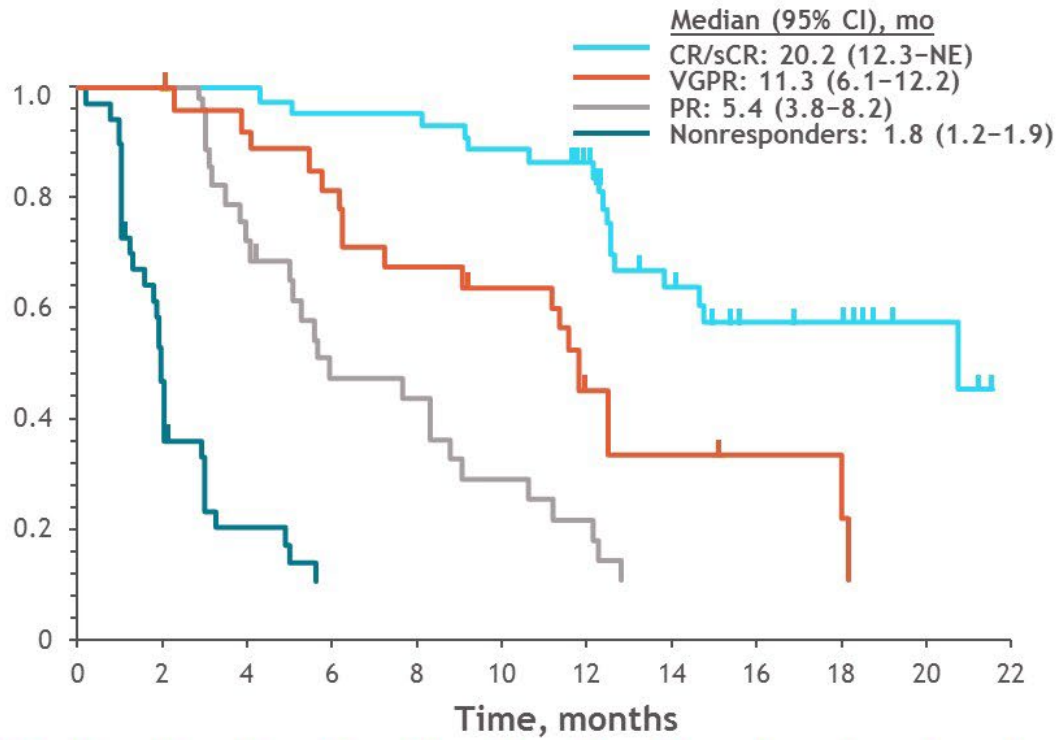
PFS by Target Dose



At risk, N												
150 × 10⁶	4	2	1	1	1	1	1	1	1	1	1	0
300 × 10⁶	70	56	42	33	29	24	17	14	11	7	2	0
450 × 10⁶	54	44	40	36	34	31	17	4	1	0	0	

- PFS increased with higher target dose; median PFS was 12 mo at 450 × 10⁶ CAR+ T cells

PFS by Best Response

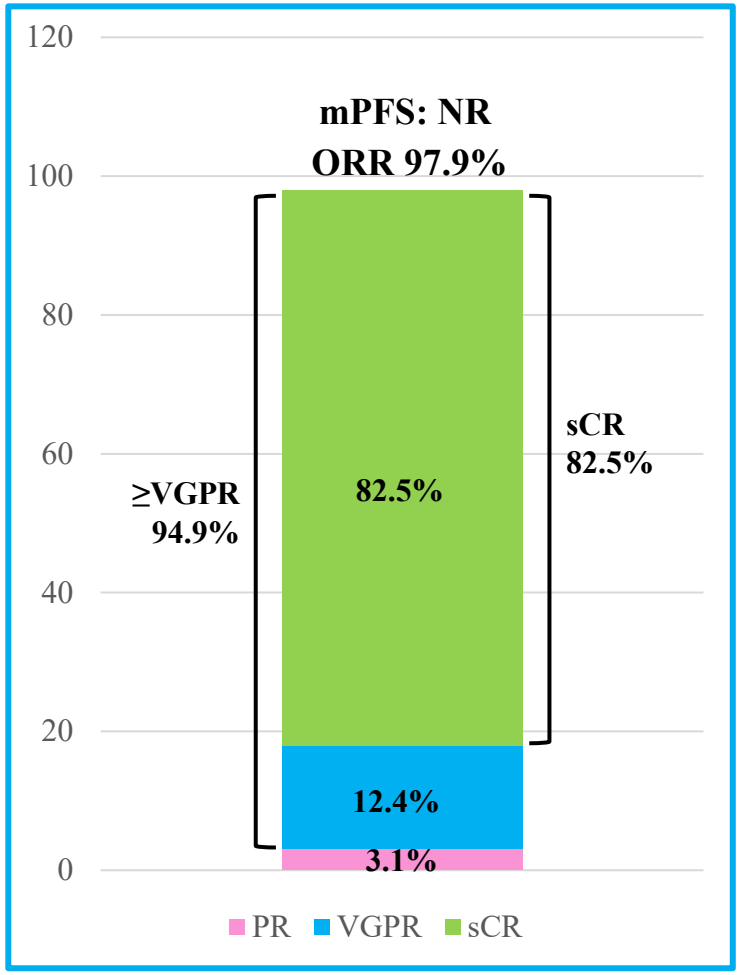


CR/sCR	42	42	42	40	39	37	26	16	11	8	4	0
VGPR	25	25	22	20	16	14	8	3	2	0	0	
PR	27	16	10	9	5	1	0	0	0	0	0	
Nonresponders	34	8	83	70	64	56	35	19	13	8	4	0

- PFS increased by depth of response; median PFS was 20 mo in patients with CR/sCR

Data cutoff: 14 Jan 2020. NE, not estimable; PFS, progression-free survival.

Ciltacabtagene Autoleucel, A B-cell Maturation Antigen (BCMA)-directed Chimeric Antigen Receptor T-cell (CAR-T) Therapy in R/R MM: Updated Results CARTITUDE-1



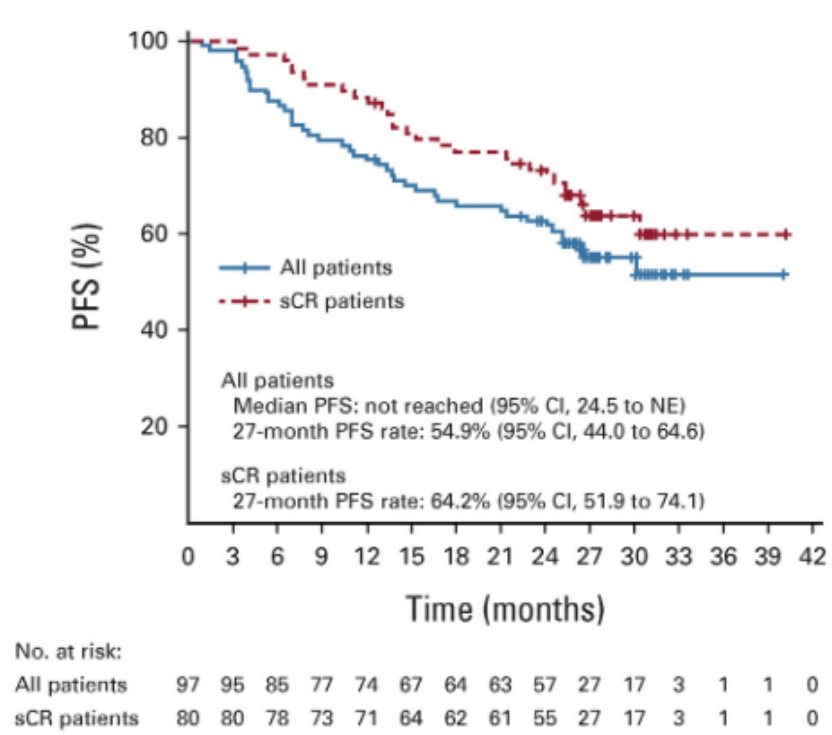
Study	Phase 1b/2
Population	• ≥3L prior therapy including PI, IMiD and anti-CD38 Ab, or double refractory or progressive disease • Overall median 6 PL therapy, 23.7% HR, 87.6% triple-class refractory, penta-refractory 42.3%, 13% had EMD, refractory to last line of Rx 99% • N=97, follow up 2 yrs post LPI
Dosing	• Range 0.5-1.0 x 10^6 CAR T-cells/kg , target dose 0.75 x 10^6 CAR T-cells/kg

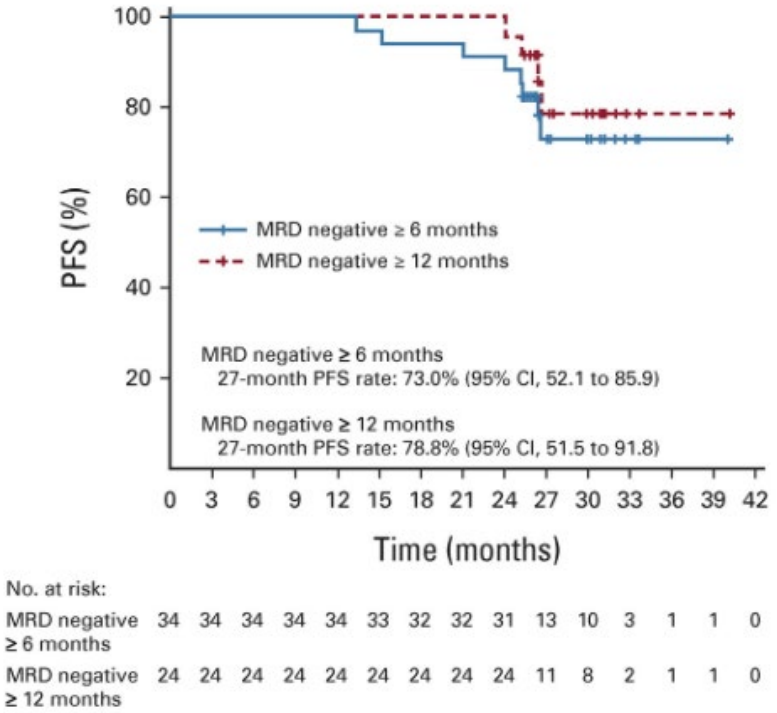
- Median time to first response: 1 month, best response in 2.6 months
- 91.8% of tested patients (N=61) were MRD –ve at 10^{-5}
- 6 month sustained MRD –ve was 68% and 12 month sustained MRD –ve in 55% of pts

Martin et al JCO 2022, 41:1265

CARTITUDE 1: PFS By Depth Of Response And Sustained MRD 10^{-5} At 6 Months And 12 Months

- mPFS and mOS NR for overall population
- 2 yr PFS rate: 55% (95% CI, 44-64.6), 2 yr PFS for sCR: 64%



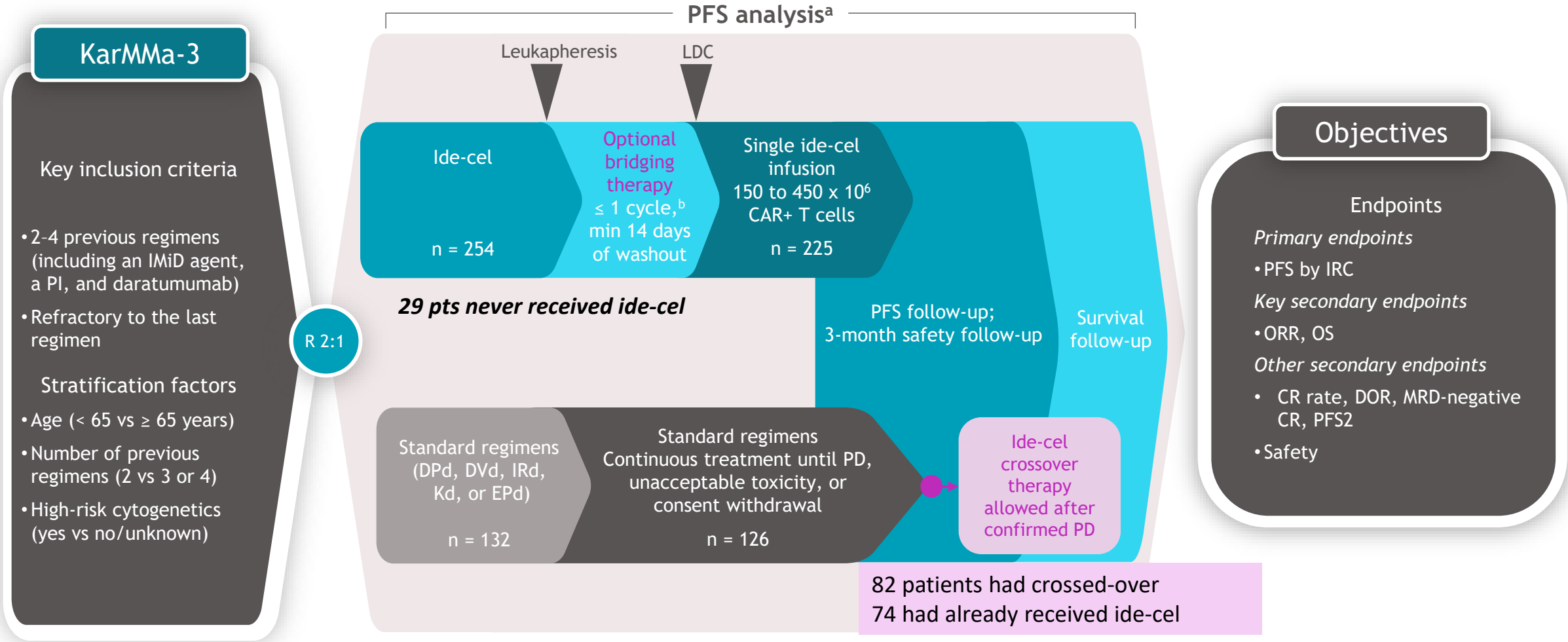


- 2 yr PFS for pts with sustained MRD –ve at 6 months was 73% and 79% for 12 month sustained MRD –ve
- 2 yr OS: 70%, with 2 yr OS in 94% and 91% respectively for sustained MRD –ve

Martin et al JCO 2022

Ph 3 KarMMa-3: ide-cel vs SoC in early line TCE RRMM (2-4 prior lines)

Study design



[a]Time from randomization to the first occurrence of disease progression or death from any cause according to IMWG criteria; [b]Up to 1 cycle of DPd, DVd, IRd, Kd, or EPd may be given as bridging therapy.
CAR, chimeric antigen receptor; CR, complete response; DOR, duration of response; DPd, daratumumab/pomalidomide/dexamethasone; DVd, daratumumab/bortezomib/dexamethasone; EPd, elotuzumab/pomalidomide/dexamethasone; IMWG, International Myeloma Working Group; IRC, Independent Response Committee; IRd, ixazomib/lenalidomide/dexamethasone; Kd, carfilzomib/dexamethasone; LDC, lymphodepleting chemotherapy; min, minimum; MRD, minimal residual disease; ORR, overall response rate; PD, progressive disease; PFS2, progression-free survival on next line of therapy; R, randomization.

Rodriguez-Otero P et al. oral presentation. ASH 2023. Abstract 1028

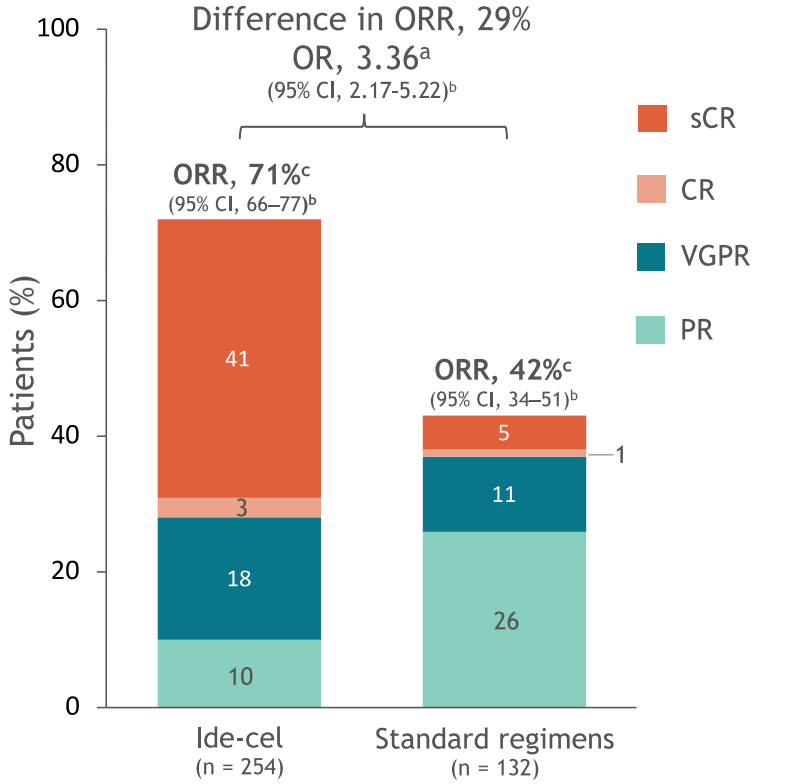
Ph 3 KarMMa-3: ide-cel vs SoC in TCE RRMM (2-4 prior lines)
Final PFS analysis and OS data (mFUP 31 m)

Key elegibility: 2-4 PL. Triple-class exposed. Refractory to last line.
Baseline characteristics were comparable between 2 arms:

- Median nº of PL: 3
- Median time from diagnosis to study entry 4 years.
- 65% of patients in both arms were triple-class refractory
- Median TTP in last regimen: 7 months

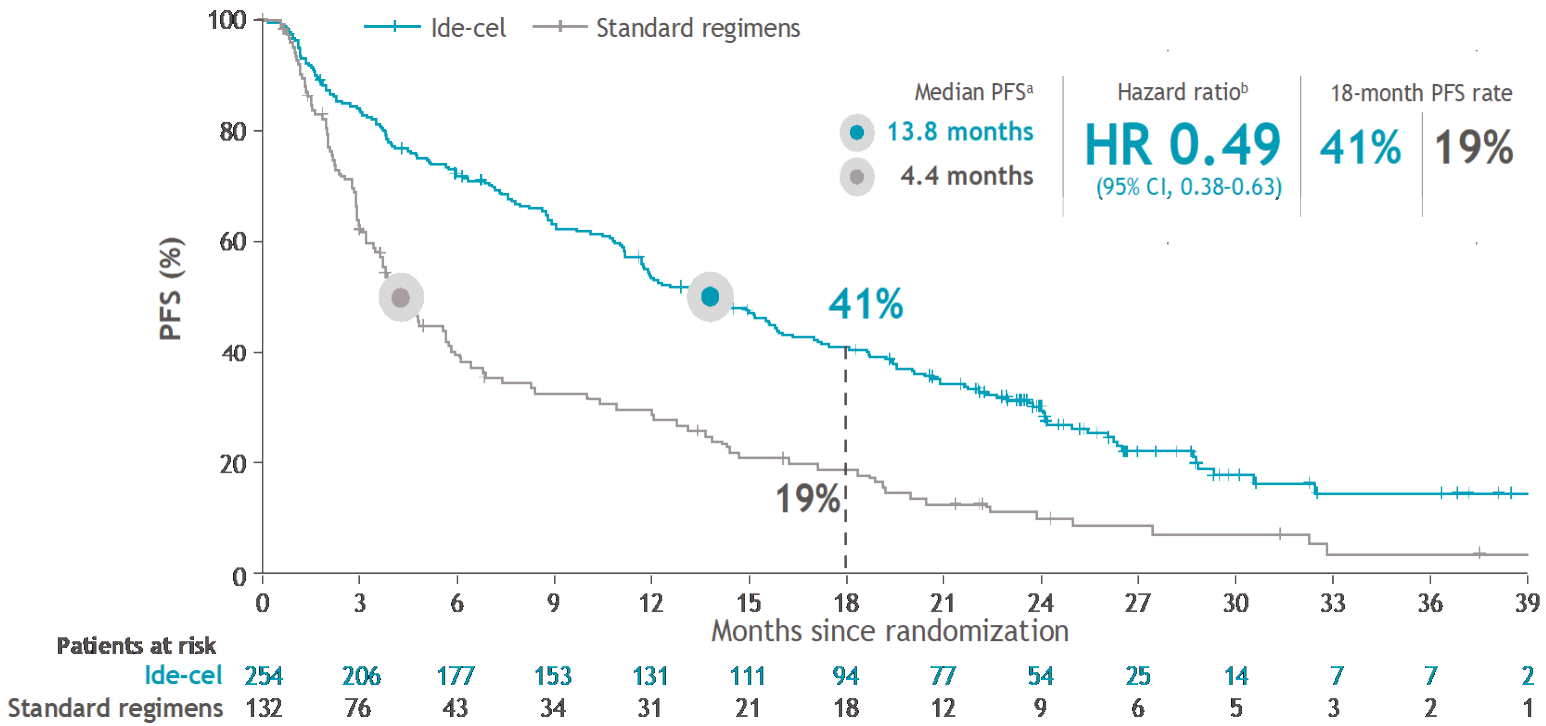
386 pts randomized:

- 254 asigned to ide-cel (=ITT population) (225 infused) [91 ongoing for PFS]
- 132 asigned to standard regimen arm (SoC) / 126 treated (DPd in 43) [20 ongoing for PFS]



- mDOR ide-cel (16.6m [12.0–18.6] vs SoC 9.7 [5.4–16.3] m)
- mTTR: 2.9 (0.5–13.0) vs 2.1 (0.9–9.4) months
- MRDneg CR: ide-cel 35% (57) vs SoC 2% (1)
- mPFS2 23.5 m vs 16.7 m [HR 0.79 (95% CI, 0.6 -1.04)]

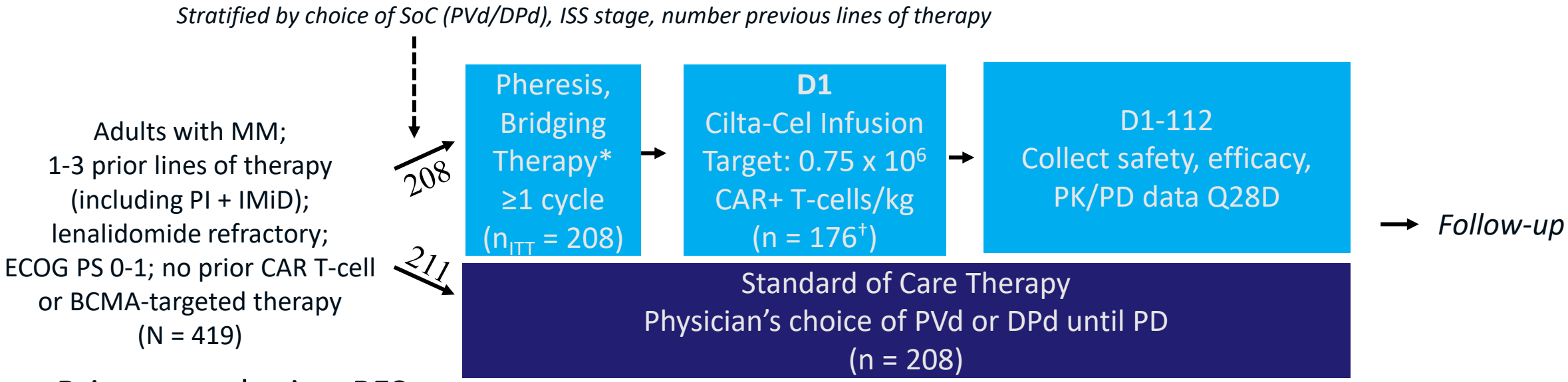
Final PFS analysis



Rodriguez-Otero P et al. oral presentation. ASH 2023. Abstract 1028

CARTITUDE-4: Phase III Trial of Cilta-Cel vs SoC in Lenalidomide-Refractory MM

- Randomized, open-label phase III trial



*Physician's choice of PVd or DPd. †As-treated population (n = 176): 32 patients did not receive cilta-cel as part of study due to PD (n = 30) or death (n = 2) during bridging therapy/lymphodepletion.

Primary endpoint: PFS

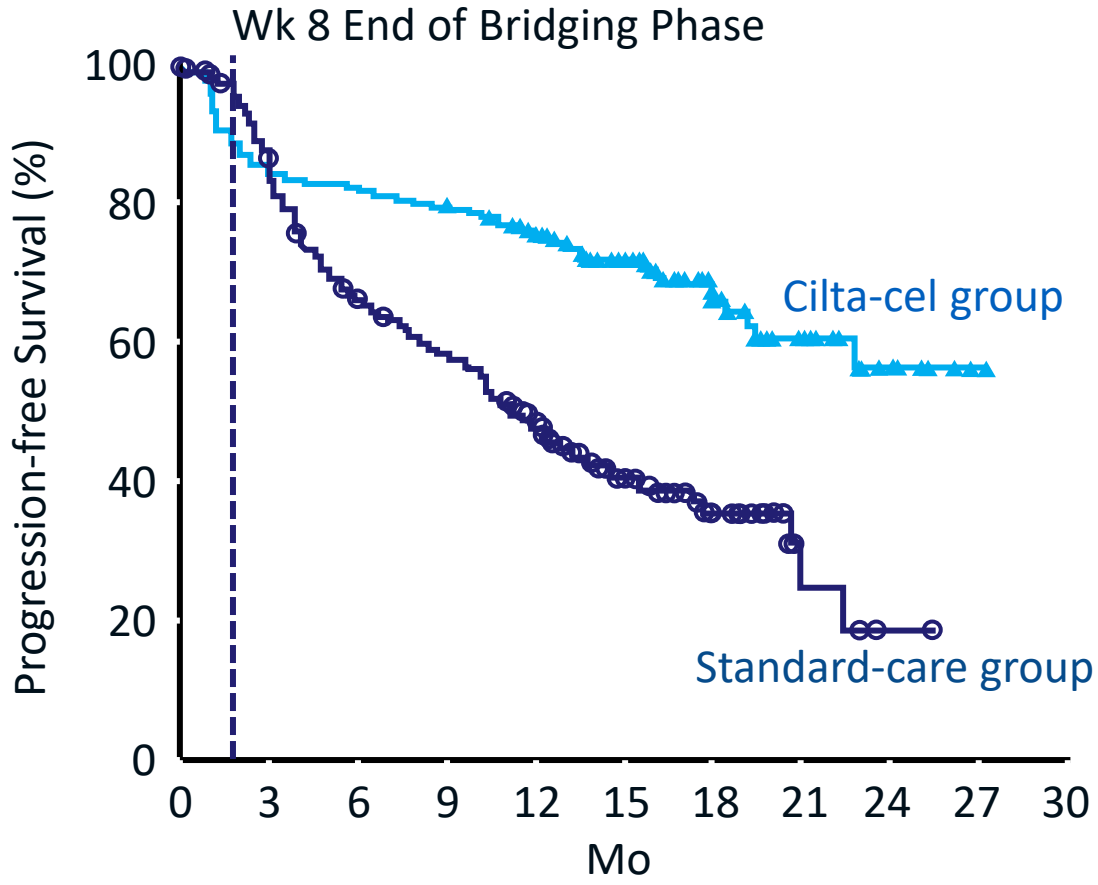
Secondary endpoints: ≥ CR, ORR, MRD negativity, OS, safety, PROs

Analysis after 15.9 mo median follow-up (range: 0.1-27 mo)

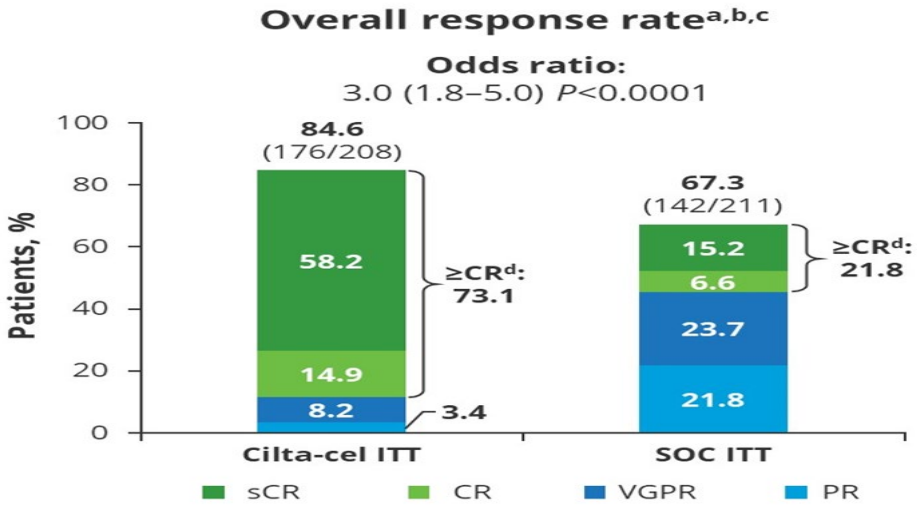
San-Miguel et al. NEJM. 2023;389(4):335-347.

CARTITUDE-4: PFS and ORR (ITT Population)

Median F/U 15.9 mos



	Cilta-Cel (n = 208)	SoC (n = 211)
mPFS, mo (95% CI)	NR (22.8-NE)	11.8 (9.7-13.8)
	HR: 0.26 (95% CI: 0.18-0.38; *P* <.0001)	
12-mo PFS, %	76	49



In subgroup analysis of PFS, all subgroups favored the Cilta-cel arm

Cilta-Cel As-Treated Population
ORR 99.4%
≥ CR 86.4%

San-Miguel et al. NEJM. 2023;389(4):335-347.

Ide-cel development plan

NDMM

TE

KarMMa-2[1], Ph 2

Cohort 2c: *≥ 3 cycles induction with PI, IMiD and DEX plus suboptimal response to ASCT*

Cohort 3: *Induction and ASCT, without subsequent consolidation or maintenance*

KarMMa-9[7], Ph 3

Suboptimal response post ASCT (PR or VGPR), 4 to 6 cycles of induction therapy containing ≥ an IMiD, a PI +/- an anti-CD38,
single ASCT 80 to 120 days prior to consent

TNE

KarMMa-4[2], Ph 1

≤ 3 cycles induction with PI, IMiD and steroids

Clinical HR

KarMMa-2[1], Ph 2

Cohort 2a:
Early relapse ≤18 mo after induction, and LEN maintenance

Cohort 2b:
Early relapse ≤18 mo after PI, IMiD and DEX, no ASCT

2–5L RRMM

< triple-class exposed

KarMMa-7[6], Ph 1/2
Arm A : ide-cel + IBER
Arm A cohort 2: 1-3 prior lines with IMiD for ≥ 2 c.

KarMMa-3[4], Ph 3

ide-cel vs standard regimens
2-4 prior regimens with Dara, PI, IMiD

Min. triple-class exposed (IMiD, PI, CD38)

KarMMa-2[1], Ph 2

Cohort 1a :
≥ 3 prior regimens with PI, IMiD and anti-CD38

Cohort 1b : +
talquetamab as a bridging

4L+ RRMM

Prior PI, IMiD and anti-CD38

CRB-401[3], Ph 1

≥ 3 prior lines with PI, IMiD and DARA

KarMMa[5], Ph 2

≥ 3 prior lines with PI, IMiD and anti-CD38

KarMMa-7[6], Ph ½
Arm A: ide-cel + IBER; Arm B: ide-cel + BMS-986405

Arm A cohort 1 and Arm B : ≥ 3 prior regimens with IMiD, PI and anti-CD38

ASCT, autologous stem cell transplantation; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CD, cluster of differentiation;; Dara, daratumumab; DEX, dexamethasone; HR, high risk; IBER, iberdomide; ide-cel, idecabtagene vicleucel; IMiD, immunomodulatory drug; L, line; Len, lenalidomide; mAb, monoclonal antibody; NDMM, newly diagnosed multiple myeloma; Ph, phase; PI, proteasome inhibitor; PVd, pomalidomide, bortezomib, dexamethasone; Rd, lenalidomide and dexamethasone; RRMM, relapsed/refractory multiple myeloma; TE, transplant eligible; TNE, transplant not eligible; VRd, bortezomib, lenalidomide and dexamethasone.
1. NCT03601078. Clinicaltrials.gov. [Link]; 2. NCT04196491. Clinicaltrials.gov. [Link]; 3. NCT02658929. Clinicaltrials.gov. [Link]; 4. NCT03651128. Clinicaltrials.gov. [Link]; 5. NCT03361748. Clinicaltrials.gov. [Link]; 6. NCT04855136. Clinicaltrials.gov. [Link]; 7. NCT06045806. Clinicaltrials.gov. [Link]

CARTITUDE Trials ongoing

CARTITUDE 2
COHORT D: consolidation in pts with <CR p ASCT +len maintenance
COHORT E: ND high risk MM, no prior therapy
COHORT F: ND standard risk MM, no prior therapy

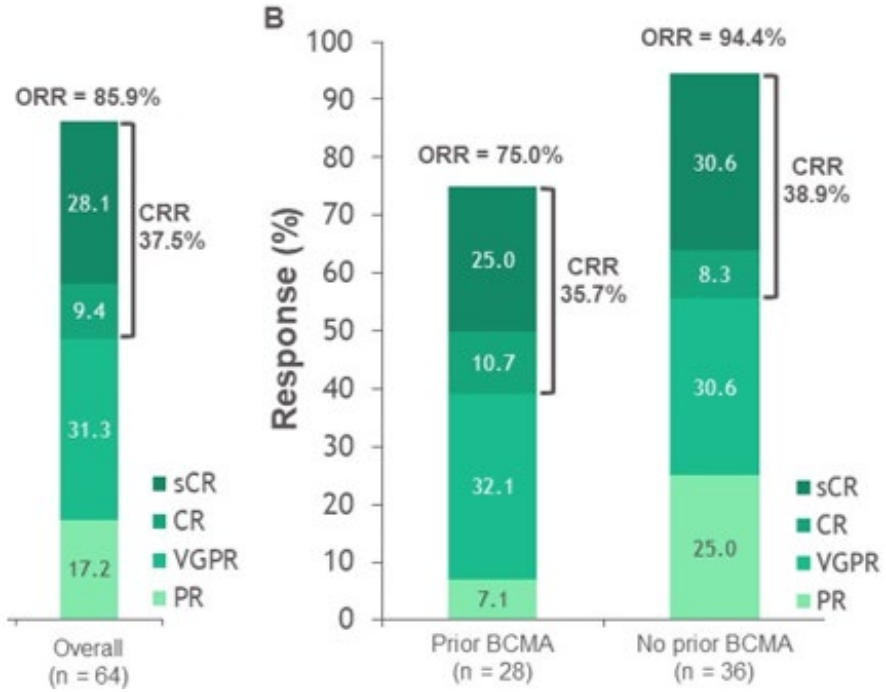
CARTITUDE-5: Randomized phase 3 of VRd f/b Cilta-Cel vs VRd f/b Rd in ND TI

CARTITUDE-6: Randomized Phase 3 Dara-VRd f/b CART vs DVRd f/b ASCT

MONUMENTAL 8: sequencing- talquetamab bridging and talquetamab consolidation in RRMM and NDMM, feasibility of pheresis post talquetamab

GPRC CART- BMS-986393

Study	GPRC CART – BMS Phase I study GPRC5D found in hair follicles, hard keratinized structures, inferior olivary nucleus
Population	PCR 34%, 46% had prior BCMA, 36% had prior BCMA CART 43% EMD, 46% HR CGA median follow up was 5.9 mo (range 0-24 mo) N=70
Dosing	Dose range 25 million to 450 million CART cells
Efficacy	ORR was 86%, CR 38%. In prior BCMA exposed was 75%.



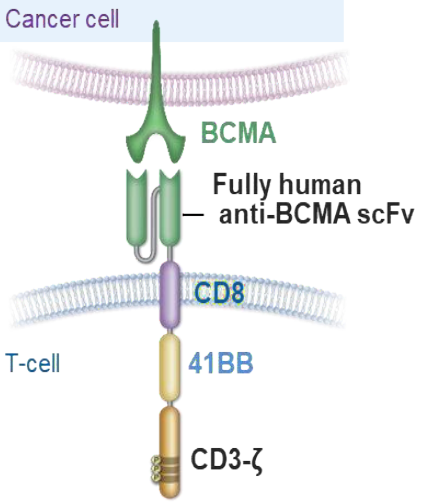
AEs	Any (%)	Gr 3/4 (%)
Infection	43	16
CRS	84	4 (1 Gr 5)
HLH	4	4
ICANS	11	3 (2 cerebellar)
Skin	24	0
Nails	16	0
Dysgeusia	3	0

PHE 885

Ph 1: PHE 885	T-Charge, an innovative platform that reduces manufacturing time to <2 days and preserves T cell stemness, results in robust expansion and prolonged CAR T cell persistence, apheresis to LD median of 16 days
Population	• ≥ 2 prior therapies, • Overall median 4 PL therapy (range 2-10) • 33% of pts had extramedullary disease; 94% were triple refractory, 62% penta ref, 90% ref to last LOT, 36% HR CGA • N=49
Dosing	• 2.5e6 (n=4), 5e6 (n=13), 10e6 (n=20), 14.3e6 (n=1), and 20e6 (n=8) CAR T cells after flu/cy or bendamustine lymphodepletion
Efficacy	• The PHE885 transgene was detected in 13/14 (93%) pts at 6 mo and 5/7 (71%) at 12 mo post infusion. • T cells with early memory phenotype were preserved in the final product and persisted in pts post infusion. • ORR 98%, MRD –ve in 6/10 evaluable patients • conversion to CR/sCR has occurred as late as 18 months after infusion in this study

	Grade 1/2 (%)	Grade 3/4 (%)	Onset (days)	Duration (days)
CRS	86	10	8	4
ICANS	14	6	10.5	-
HLH	-	6		

- Dose limiting toxicities included gr 4 lipase increase, gr 3 serum amylase increase, gr 3 transaminitis, and gr 3 reduced EF
- No reports of delayed NT or Parkinson's

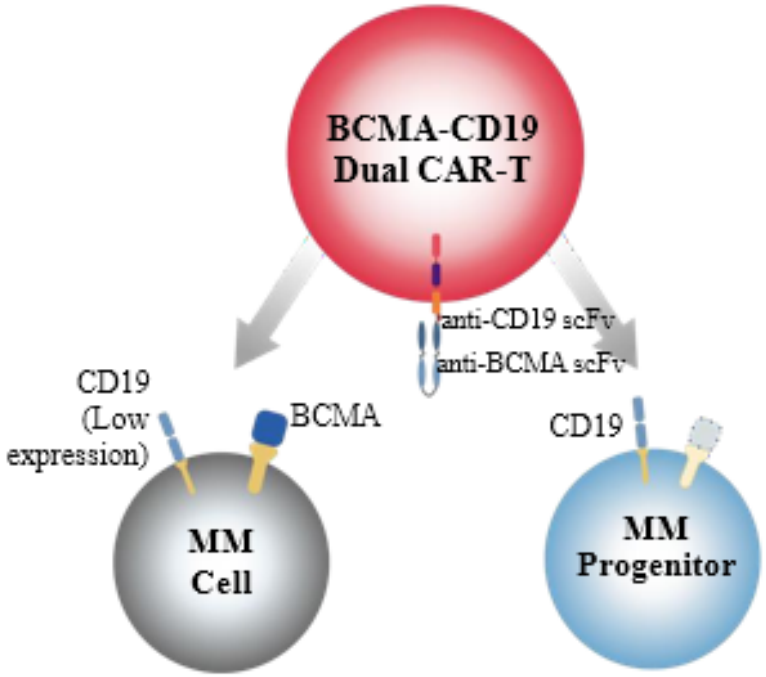


PHE855

Sperling A et al, ASCO 2023, abstract # 8004

Gracell Dual CAR-T BCMA/CD19

Ph 1	• **Proprietary FasTCAR platform, 22-36 hr manufacturing,** • **CART cells appear younger, less exhausted and show enhanced proliferation, persistence, bone marrow migration and tumor cell clearance activities as demonstrated in preclinical studies.** • **Combines 3 production steps- activation, transduction and expansion into a single concurrent activation-transduction step**
Population	• > 3 prior therapies, including PI, IMiD, anti CD38 and refractory to last line • Overall median 5 PL therapy; 90% pts were high risk, 28% had EMD, 83% refractory to last therapy, 62% penta exposed. • N=29
Dosing	• 3 dose levels: 1x10^5/kg (DL1) n=2, 2x10^5/kg (DL2) n=10 and 3x10^5/kg (DL3) n=17
Efficacy	• Median f/u 30.7 mo (range 14.6-43.6 mo) • ORR 93%, 83% CR/sCR • 83% MRD –ve sCR, 78.6% of evaluable patients were MRD-ve at 12 mo • mDOR 37 mo, mPFS 38 mo



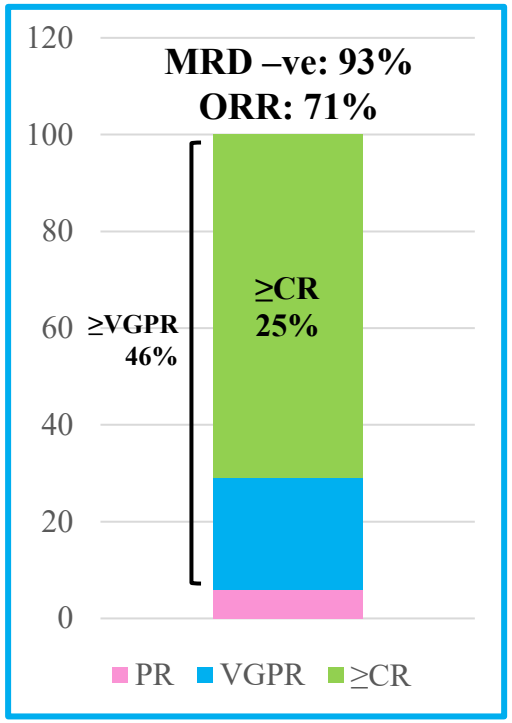
	Grade 1/2 (%)	Grade 3/4 (%)	Duration (days)
CRS	79	7	3
ICANS	0	0	-

Du et al. ASCO 2023, abstract

Allo CART

Ph 1	**Engineered to abrogate GVHD and CART rejection Using TALEN gene editing to knock out TCRa constant region to eliminate GVHD and CD52 knock out to use allo 647 an anti CD52 Ab to LD host T cells to prevent rejection.**
Population	• ≥3 prior lines of therapy; no bridging therapy allowed • All pts refractory to last line; 37% HR, 21% EMD, 19% ISS stage III • Median 5 PL of therapy; 91% TCR, 42% penta refractory • N=43, median time to treatment was 5 days
Dosing	• ALL0-715 allogeneic product, Optimal dose of 320 million CAR T cells and flu/cy/ALLO-647 (anti-CD52 mAb for lymphodepletion)
Efficacy	• Median f/u 10.2 months • median DOR of 8.3 months

Median f/u 10.2 mo



	Any Grade (%)	Grade 3/4
CRS	56	2
ICANS	14	-

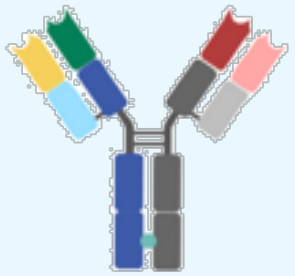
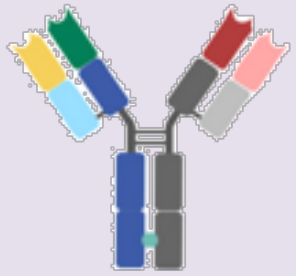
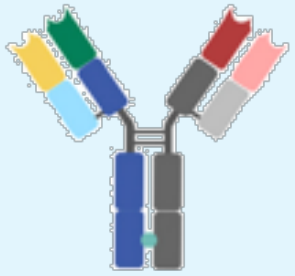
- Most common Grade (Gr) 3+ adverse events (AEs) included anemia, neutropenia, lymphopenia, and thrombocytopenia.
- No GvHD, 28% grade 1 or 2 IRRs
- Infections in 54%, Gr 3+ infections occurred in 23% of pts, including 3 Gr 5 events (fungal pneumonia and adenovirus hepatitis)

Mailankody et al, Nature Medicine 2023, 29:422

Bispecific Antibody	Alnuctamab (CC-93269)[1]	Erlantamab[2]	Linvoseltamab[3]	Teclistamab[4]	TNB-383B[5]	Anti-GPRC5d Talquetamab[6]	Anti-FcRH5 Cevostamab[7]
Treatment	SC D1,4,8,15,22 C1, QW C2-3, Q2W C4-6, Q4W C7-beyond.	Weekly SC	Weekly IV	Weekly SC	IV q3w	SQ	IV q3w
Patients	n= 47	n=55	n=252 (Ph1 = 73; Ph2 = 179)	n=165	n= 60 (≥ 40 mg)	n= 143 (0.4m/kg qwk), n = 145 (0.8 mg/kg q2wk)	n= 160
Median prior lines	4	5	5	5	5	6/5	6
Triple-class refractory	62%	91%; 24% prior BCMA-directed	81%	78%	65%	74%/69%	85%
ORR @	10/13 (77%)	64%	64%	63%	79% (n=24 mature)	74%/73%	55% (160 mg) 37% (90mg)
therapeutic dose	≥ 30 mg SC	215-1000 µg/kg SC	200 mg cohort (n=58)	1.5 mg/kg SC	≥ 40 mg		
Duration of Response	NR	17.1 m	NR	18.4 months			15.6 months
AEs, (All %/(Gr 3+%)							
	89% (62%)		95% (66%)	100% (95%)	77% (32%)	79%/75%	99% (59%)
CRS	53% (0%)	67% (0%)	37% (1%)	72% (1%)	52% (3%)	58%/65%	80% (1.3%)
Infections				76% (45%)	28%		43% (19%)
Neutropenia	34% (30%)			71% (64%)	17%	ICANS 11%-11%	18% (16%)
Anemia	34% (17%)		28% (24%)	52% (37%)		Skin-related AEs 56%-71%	32% (22%)
Thrombocytopenia				40% (21%)			
Deaths (n/%)					Deaths 5 (5%)	Nail-related AEs 54%-53%	Deaths 1pt (0.6%)
Other		ICANS 0% (0%)	ICANS 2% (2%)	Neurotox 15% (1%) ICANS 3 (0%)		Dysgeusia 50%-48%	Neurological/Psychiatric 41% (4%)

Overview of Approved Bispecific Antibodies in Multiple Myeloma

Approved bispecific antibodies in the management of relapsed/refractory multiple myeloma

	Teclistamab (anti-BCMA)	Talquetamab (anti-GPRC5D)	Elranatamab (anti-BCMA)
	IgG1 Fc	IgG1 Fc	IgG2a Fc
			
Approved:	**10/25/2022**	**8/9/2023**	**8/14/2023**

All indicated for use in R/R MM with ≥4 prior lines of therapy, including

- Proteasome inhibitor
- Immunomodulatory agent
- Anti-CD38 monoclonal antibody

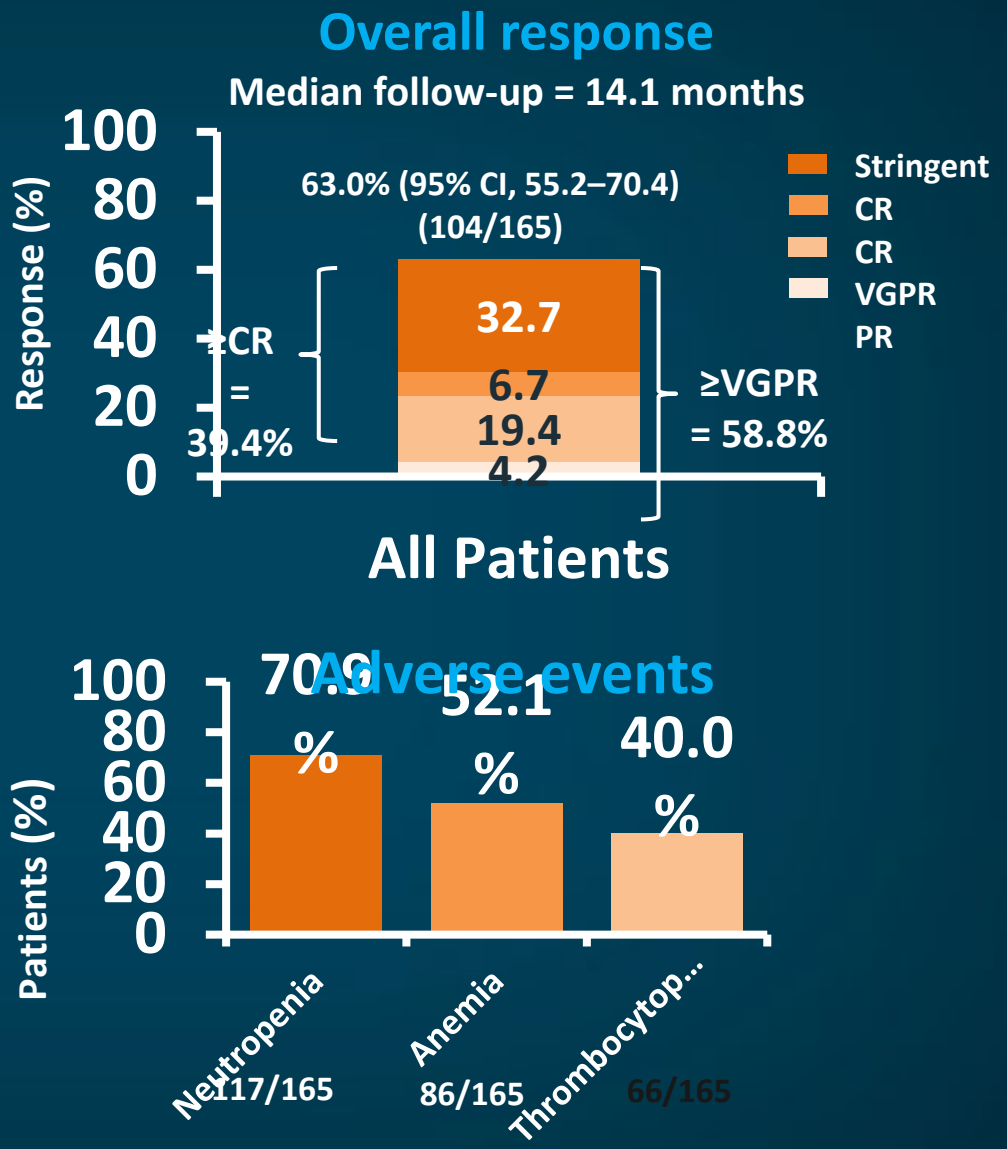
- Teclistamab was approved 10/25/2022 for use in adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody
- Talquetamab was approved 8/9/2023 for adults with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody
- Elranatamab was approved 8/14/2023 for use in adults with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody

Fab = fragment antigen binding; Fc = fragment crystallizable (region); ; FcRH5 = Fc receptor-homolog 5; FcRL5 = Fc receptor-like protein 5; IgG = immunoglobulin G.

Cho SF, et al. *Front Oncol*. 2022;12:1032775. FDA news release 10/25/2022 (www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-teclistamab-cqyv-relapsed-or-refractory-multiple-myeloma). FDA news release 8/14/2023 (https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-elranatamab-bcmm-multiple-myeloma). FDA news release 8/9/2023 (https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-talquetamab-tgvs-relapsed-or-refractory-multiple-myeloma). URLs accessed 11/4/2023.

Teclistamab: MajesTEC-1 Trial Efficacy Results

- **MajesTEC-1**
  - 2 step-up doses of 0.05 mg/kg and 0.3 mg/kg; then 1.5 mg/kg SC weekly
  - ORR = 63.0%; 39.4% had CR or better
  - Median DoR = 18.4 months
  - Median PFS = 11.3 months
- Separate study (n = 38) with prior BCMA-targeted treatment, ORR = 40%
  - 26% developed grade 3 to 4 infections
- **Safety**
  - Cytokine release syndrome = 72.1%; grade 1 (50.3%), grade 2 (21.2%)
    - 33% of patients had ≥2 CRS events
    - 36.4% of patients with CRS required tocilizumab



CI = confidence interval; PR = partial response; SC = subcutaneous(ly); VGPR = very good partial response.

Moreau P, et al. *N Engl J Med*. 2022;387:495-505. Touzeau C, et al. *J Clin Oncol.* 2022;40(16 suppl); Abstract 8013. FDA news release 10/25/2022 (www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-teclistamab-cqyv-relapsed-or-refractory-multiple-myeloma). Accessed 11/4/2023. Teclistamab [Package Insert]. https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=54e0f974-ccee-44ea-9254-40e9883cee1e.

Elranatamab: MagnetisMM-3 Update

- Among responders, median TTR = 1.2 mo (0.9–7.4)
  - Median DOT= 5.6 mo (0.03–19.8)
  - Median DOR NE (12 mo–NE)
  - Probability of maintaining response at 6 mo was 90.4% (95% CI, 79.8–95.6)
- **Safety**
  - TEAEs occurring in ≥20% of patients
  - CRS events all grade 1 (42.0%) or grade 2 (14.3%)
    - 98.8% with first 3 doses, and 90.6% with step-up dose
    - ≥ 1 CRS event in 18 patients (15.1%)
    - Treated with tocilizumab (22.7%) and corticosteroids (8.4%)
  - ICANS in 4 of 119 (3.4%) patients, all events of grade 1/2
    - Supportive treatment with corticosteroids (1.7%), tocilizumab (1.7%), and levetiracetam–seizure prophylaxis (0.8%)
  - No permanently discontinuation due to CRS or ICANS

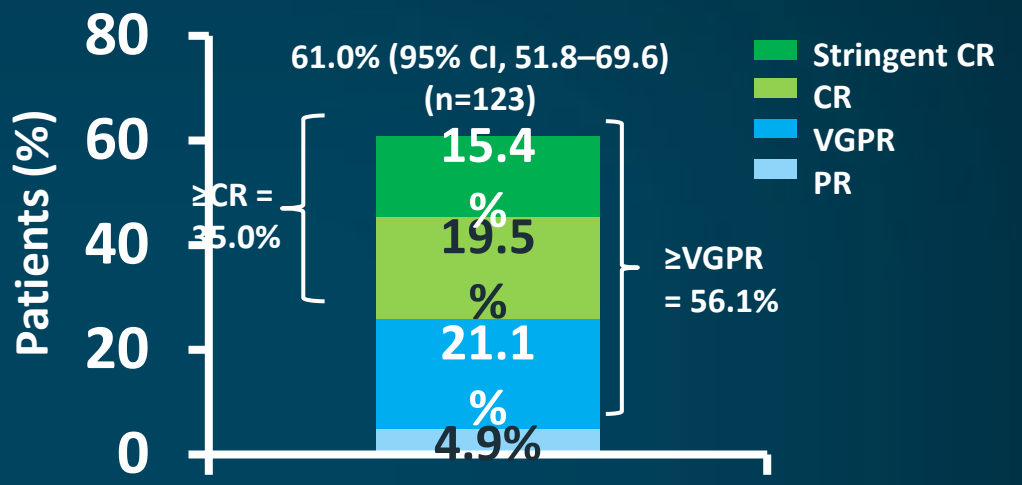
[a] Preferred terms included in hematologic TEAEs are provided in Supplementary Table 2 of Lesokhin et al.

TTR = time to objective response; DOT = duration of treatment; NE = not evaluable/estimable; TEAE = treatment-emergent adverse event.

Bahlis NJ, et al. ASH 2022; Abstract 159. Lesokhin AM, et al. *Nat Med*. 2023;29(9):2259-2267.

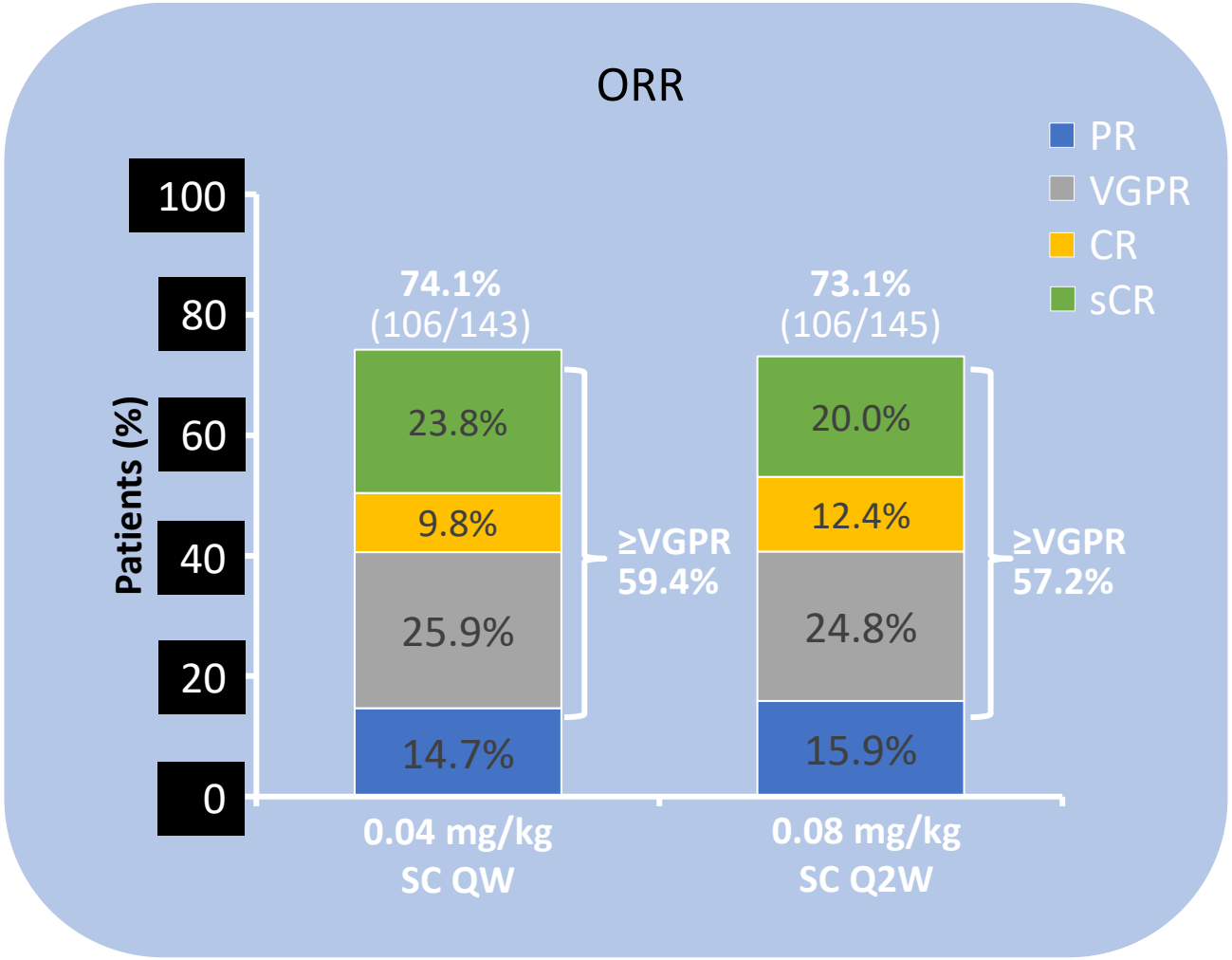
Overall response

Median follow-up = 14.7 months (range 0.2-25.1 months)



TEAEs, n (%)	Any grade	Grade 3/4
Any TEAE	123 (100)	87 (70.7)
Hematologic[a]		
Anemia	60 (48.8)	46 (37.4)
Neutropenia	60 (48.8)	60 (48.8)
Thrombocytopenia	38 (30.9)	29 (23.6)
Lymphopenia	33 (26.8)	31 (25.2)
Nonhematologic		
Cytokine release syndrome	71 (57.7)	0
Diarrhea	52 (42.3)	2 (1.6)
Fatigue	45 (36.6)	4 (3.3)
Decreased appetite	41 (33.3)	1 (0.8)
[illegible]	32 (26.0)	13 (10.6)

MonumenTAL-1: ORR

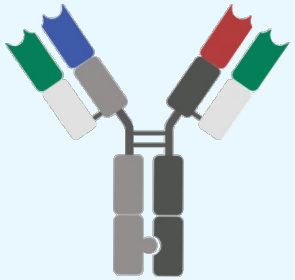
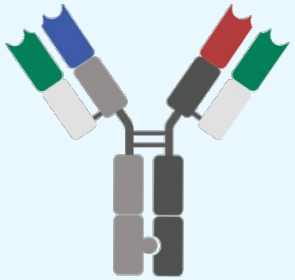
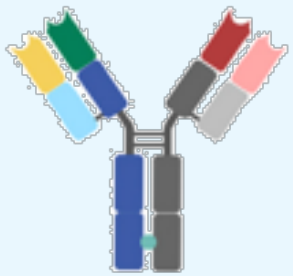
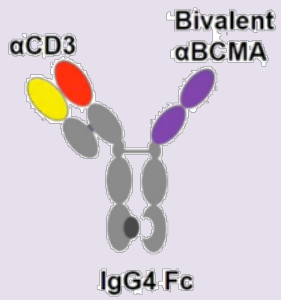
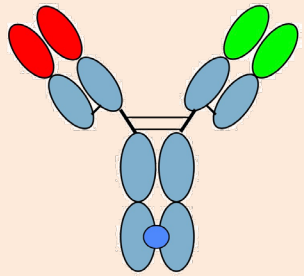
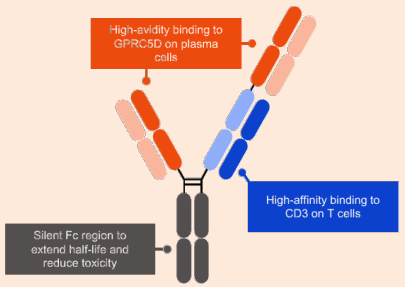


- Similar ORR among all subgroups examined, including refractory status, except for patients with BL plasmacytoma
- ORR was similar for both dosing schedules
  - Triple-class refractory: 72.6% (63.1-80.9) QW and 71.0% (61.1–79.6) Q2W
  - Penta-drug refractory: 71.4% (55.4–84.3) QW and 70.6% (52.5–84.9) Q2W

Timing	0.4 mg/kg SC QW (n = 143)	0.8 mg/kg SC Q2W (n = 145)
Median follow-up for efficacy, mo (range)	14.9 (0.5-29.0)	8.6 (0.2-22.5)
Median time to first response, mo (range) (n = 106 in each group)	1.2 (0.2-10.9)	1.3 (0.2-9.2)
Median time to best response, mo (range) (n = 106 in each group)	2.2 (0.8-12.7)	2.7 (0.3-12.5)

Chari. ASH 2022. Abstr 157.

Overview of Investigational Bispecific Antibodies in Multiple Myeloma

Linvoseltamab (anti-BCMA)	REGN5459 (anti-BCMA)	Alnuctamab (anti-BCMA)	TNB-383B (anti-BCMA)	Cevostamab (anti-FcRL5/FcRH5)	Forimtamig (anti-GPRC5D)
Fc region Fab arms	Fc region Fab arms	IgG1 Fc	IgG4 Fc	IgG1 Fc	Silent Fc region
					

Fab = fragment antigen binding; Fc = fragment crystallizable (region); FcRH5 = Fc receptor-homolog 5; FcRL5 = Fc receptor-like protein 5; GPRC5D = G protein–coupled receptor, class C, group 5, member D; IgG = immunoglobulin G.

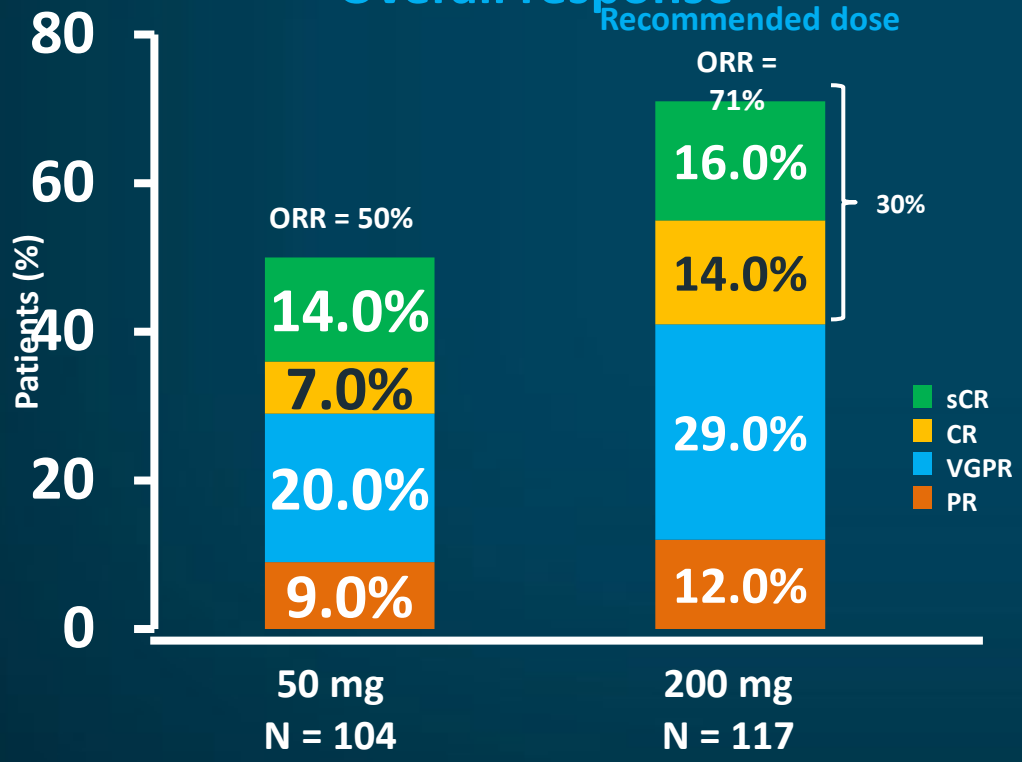
Cho SF, et al. *Front Oncol*. 2022;12:1032775. Hosny M, et al. *J Clin Med*. 2021;10(19):4593. Hasselbalch Riley AC. European Hematology Association (EHA) 2022; Abstract 1580.

Linvoseltamab (REGN5458): LINKER-MM1

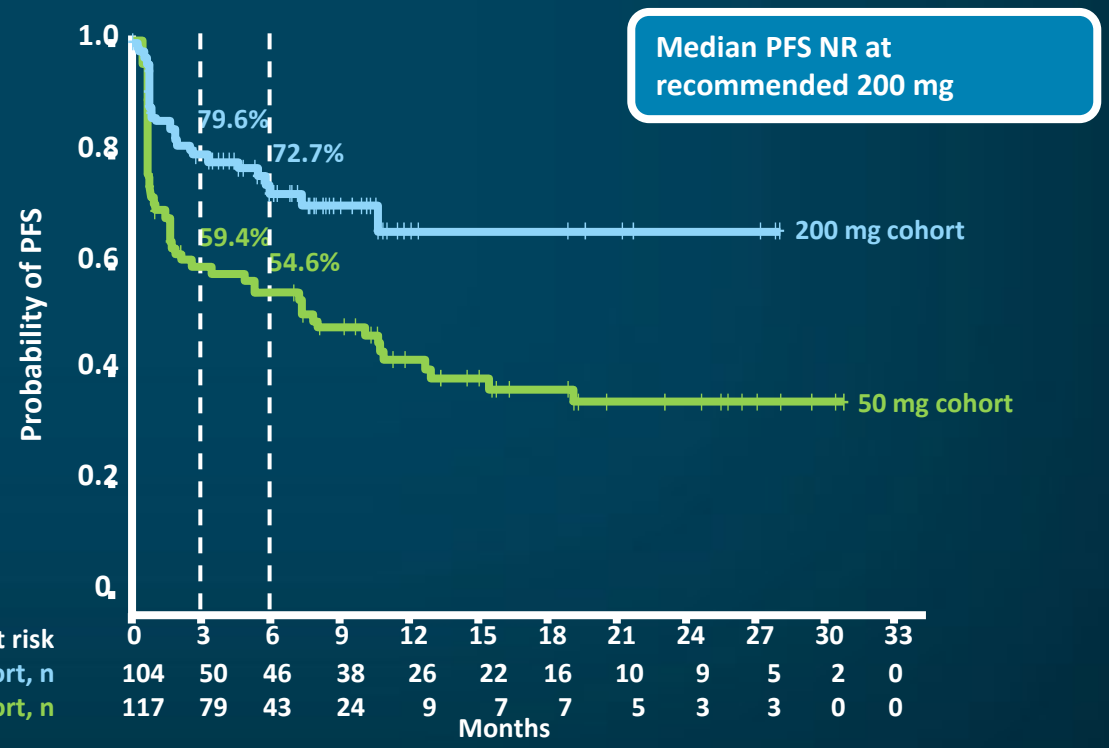
Phase 2 ORR and PFS at 50 mg and 200 mg dose regimens; BCMA x CD3

- Median age 65 years (50 mg, n = 104) and 70 years (200 mg, n = 117)
- ≥3 prior lines including anti-CD38 Ab, PI, and IMiD or ≥ triple class refractory
- Median DoR at 50 mg = 7.7 months (0.3–31.3) and at 200 mg = 5.6 months (0.2–28.2)

Overall response†



PFS 50 mg and 200 mg cohorts

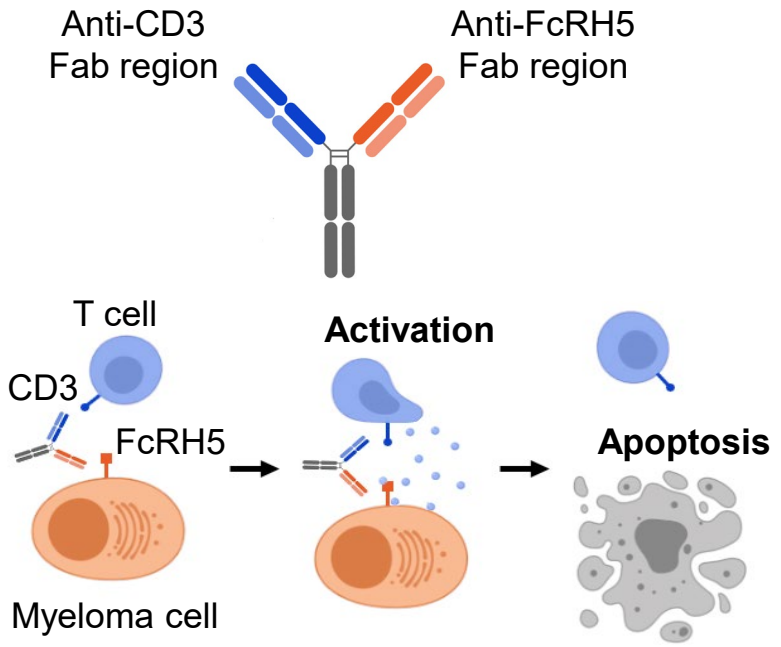


Richter J, et al. International Myeloma Society (IMS) 2023; Poster P-044 (https://imsannual2023.eventscribe.net/fsPopup.asp?efp=T0dKRktCQkMxMzg1OA&PosterID=604868&rnd=0.27828&mode=posterInfo). Accessed 11/4/2023.

Cevostamab: FcRH5×CD3 bispecific antibody

- Fc receptor-homolog 5 (FcRH5)
  - expressed exclusively in B-cell lineage (myeloma cells > normal B cells)[1]
  - near ubiquitous expression on myeloma cells[1,2]
- Cevostamab bispecific antibody
  - targets membrane-proximal domain of FcRH5 on myeloma cells and epsilon domain of CD3 on T cells[1]
  - dual binding results in T cell-directed killing of myeloma cells[1]
- Promising activity in a Phase I dose-finding study* in patients with heavily pre-treated RRMM, including those with prior exposure to BCMA-targeted agents[3]

Cevostamab structure and mode of action



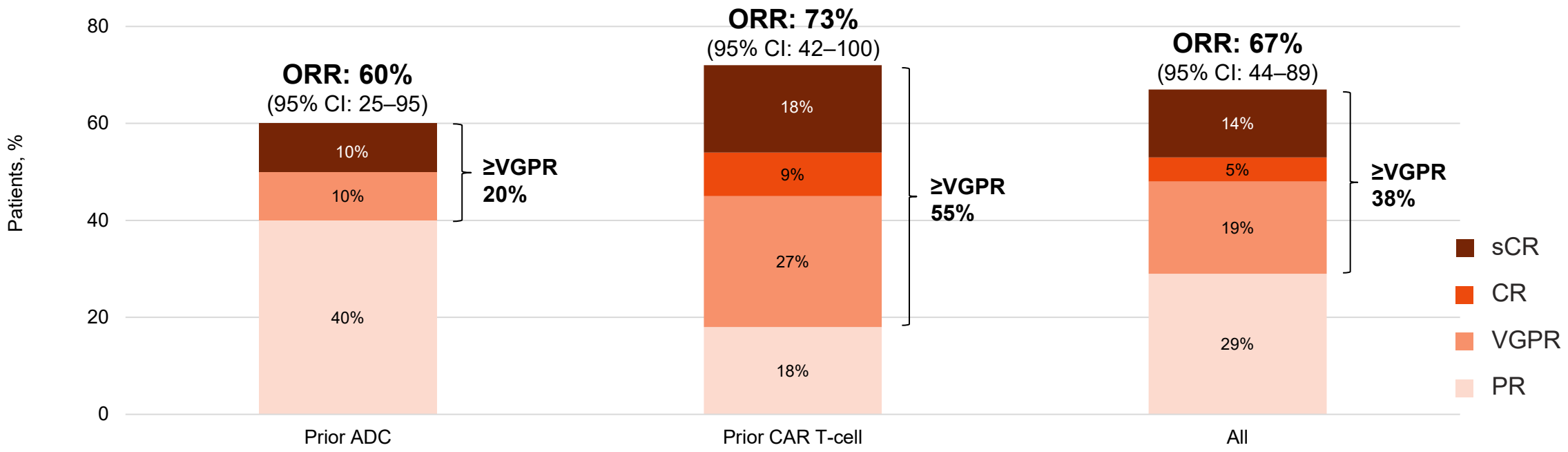
Aim: present initial results from a Phase I/II study† evaluating the efficacy and safety of cevostamab in patients with RRMM who are triple-class refractory and have received a prior BCMA-targeted agent

*NCT03275103; †NCT05535244; BCMA, B-cell maturation antigen; Fab, fragment antibody binding; RRMM, relapsed/refractory multiple myeloma

1. Li J et al. Cancer Cell 2017;31:383–95;
2. Sumiyoshi T et al. EHA 2021; 3. Trudel S et al. ASH 2021.

Response rates

Response rates among efficacy evaluable patients

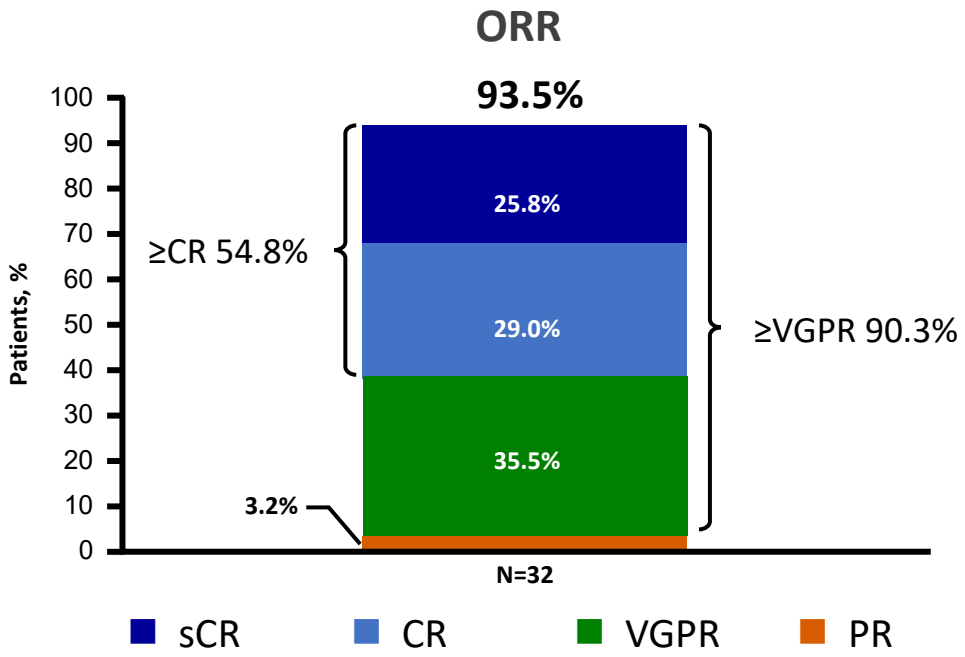


Median time to first response was xx (range: xx–xx) with a median time to CR of xx (xx–xx)
At data cut-off, xx/xx responders were still in response

Data cut-off: February 23, 2024; CI, confidence interval; CR, complete response; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

MajesTEC-2: Can Teclistamab Be Combined With Dara?

- Ph1b study
- 1-3 prior LOT including an IMiD and PI
- Cohort E: Weekly doses of teclistamab (0.72 or 1.5 mg/kg with step-up dosing) plus Dara and Len

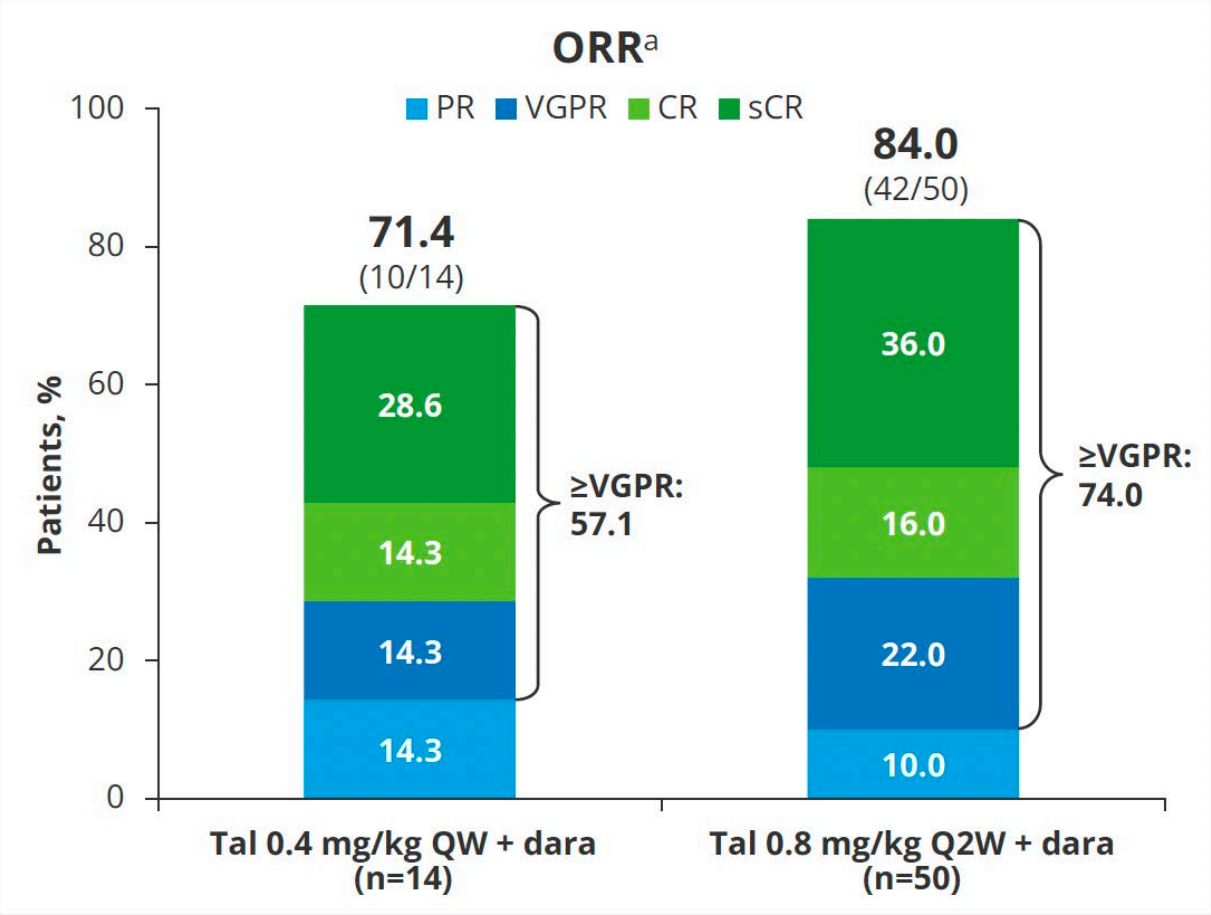


AE (any Grade: ≥25% and/or Grade 3/4: ≥3.1%), n (%)	N=32	
	Any Grade	Grade 3/4
Patients with ≥1 infection, n (%)	29 (90.6)	12 (37.5)
COVID-19	12 (37.5)	4 (12.5)
Upper respiratory infection	10 (31.3)	0
Pneumonia	8 (25.0)	5 (15.6)
COVID-19 pneumonia	4 (12.5)	1 (3.1)
Sepsis	3 (9.4)	3 (9.4)
Pneumonia pseudomonal	2 (6.3)	2 (6.3)
Cytomegalovirus infection	2 (6.3)	2 (6.3)

- Infections were common, mostly low-grade
- 2 fatal AEs reported, unrelated to teclistamab
  - COVID-19
  - Multi-organ failure due to sepsis

Searle E et al. ASH 2022: Abstract 160.

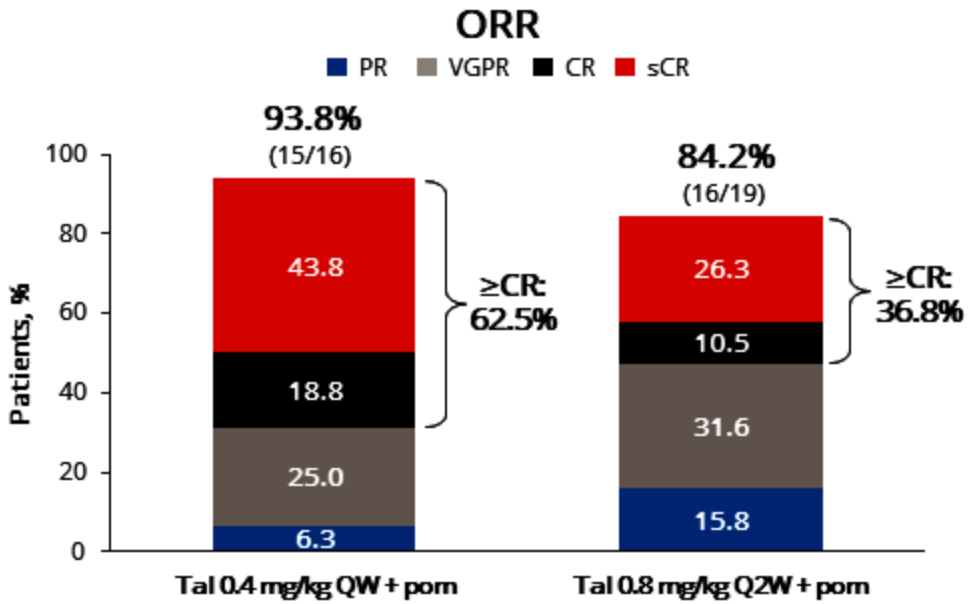
TRIMM-2 (Tal + Dara): Deep Responses With Longer Follow-Up



Parameter	Tal 0.4 mg/kg QW + dara (n=14)	Tal 0.8 mg/kg Q2W + dara (n=51)
Median (range) follow-up, mo	16.8 (1.9–31.0)	15.0 (1.0–23.3)
Median (range) time to first response, mo	1.0 (0.9–2.4)	1.0 (0.9–8.3)
ORR in anti-CD38, n (%)		
Naïve	3/3 (100.0)	5/5 (100.0)
Exposed	7/11 (63.6)	37/45 (82.2)
Refractory	7/11 (63.6)	32/40 (80.0)
ORR in T-cell redirection therapy[b] exposed, n (%)	4/6 (66.7)[c]	15/19 (78.9)
CAR-T	1/2 (50.0)	8/9 (88.9)
BsAb	4/5 (80.0)	7/10 (70.0)

Data cut-off: April 6, 2023.
[a]Response was assessed by investigators in response-evaluable patients, based on IMWG criteria. Percentages may not total due to rounding. [b]Prior T-cell redirection therapy includes BCMA and non-BCMA bispecific antibody or CAR-T therapies. [c]One patient received BsAb and CAR-T therapy.
BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T cell; CR, complete response; dara, daratumumab; IMWG, International Myeloma Working Group; ORR, overall response rate; PR, partial response; Q2W, every other week; QW, weekly; sCR, stringent complete response; tal, talquetamab; VGPR, very good partial response.

MonumenTAL-2 (Tal+Pom): High ORR With Rapid and Deep Responses



	Tal 0.4 mg/kg QW + pom (n=16)	Tal 0.8 mg/kg Q2W + pom (n=19)
Median follow-up, months (range)	15.0 (1.2–19.0)	11.1 (1.2–14.8)
Median time to first response, months (range)	1.7 (0.9–3.3)	1.2 (0–4.8)

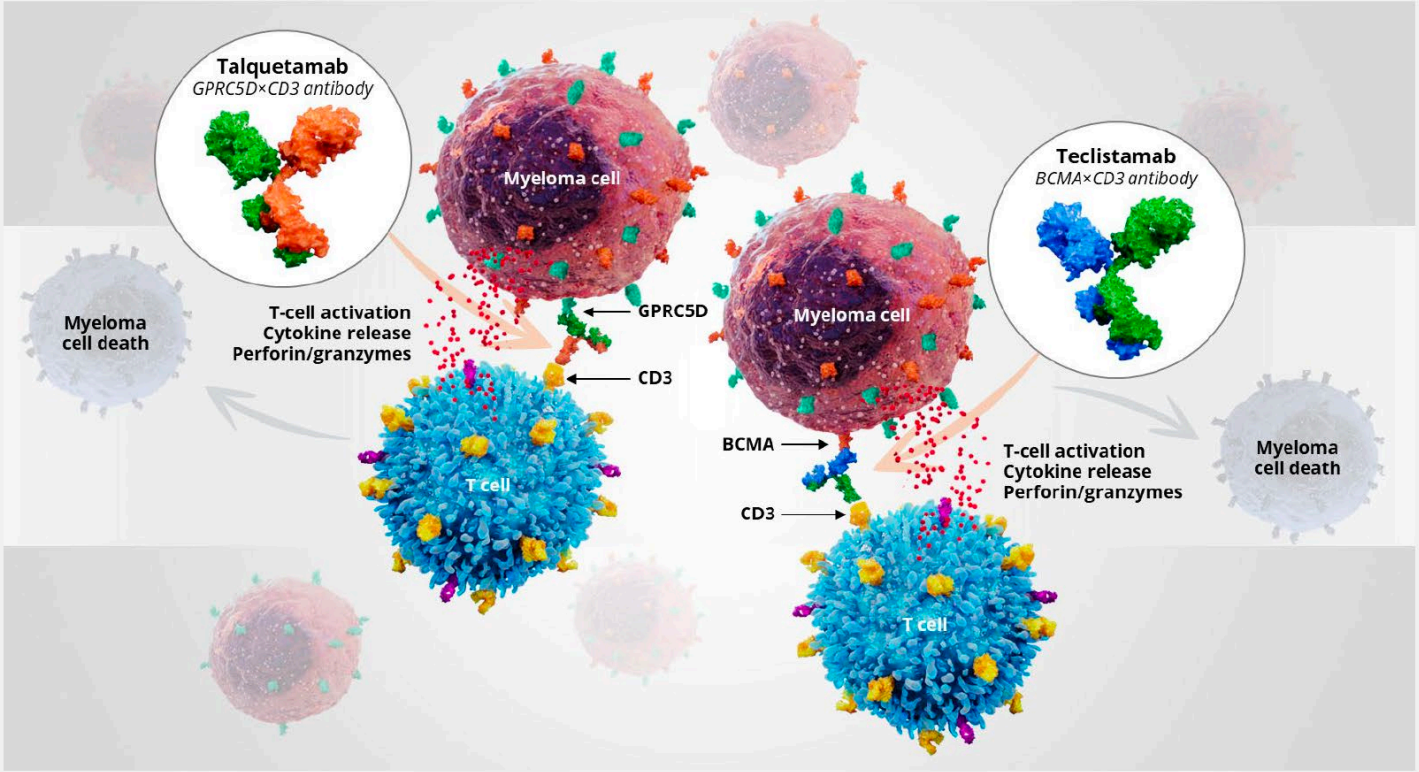
- ORRs were consistent across patient subgroups
  - 100% (3/3) in CAR-T–exposed patients in the QW cohort (no patients had CAR-T exposure in Q2W)
  - 100% (5/5 in QW, 3/3 in Q2W) in pomalidomide-exposed patients in both cohorts
  - 50% (1/2 in QW) and 67% (2/3 in Q2W) in patients with EMD
  - 80% (4/5 in QW) and 75% (3/4 in Q2W) in patients with high-risk cytogenetics

Data cut-off date: October 11, 2023.
CAR, chimeric antigen receptor; CR, complete response; EMD, extramedullary disease; ORR, overall response rate; pom, pomalidomide; PR, partial response; Q2W, every other week; QW, weekly; sCR, stringent complete response; tal, talquetamab; VGPR, very good partial response.

Presented by J Matous at the 65th American Society of Hematology (ASH) Annual Meeting; December 9–12, 2023; San Diego, CA, USA

Teclistamab and Talquetamab: First Combination of Bispecific Antibodies to Target 2 Distinct Myeloma Antigens

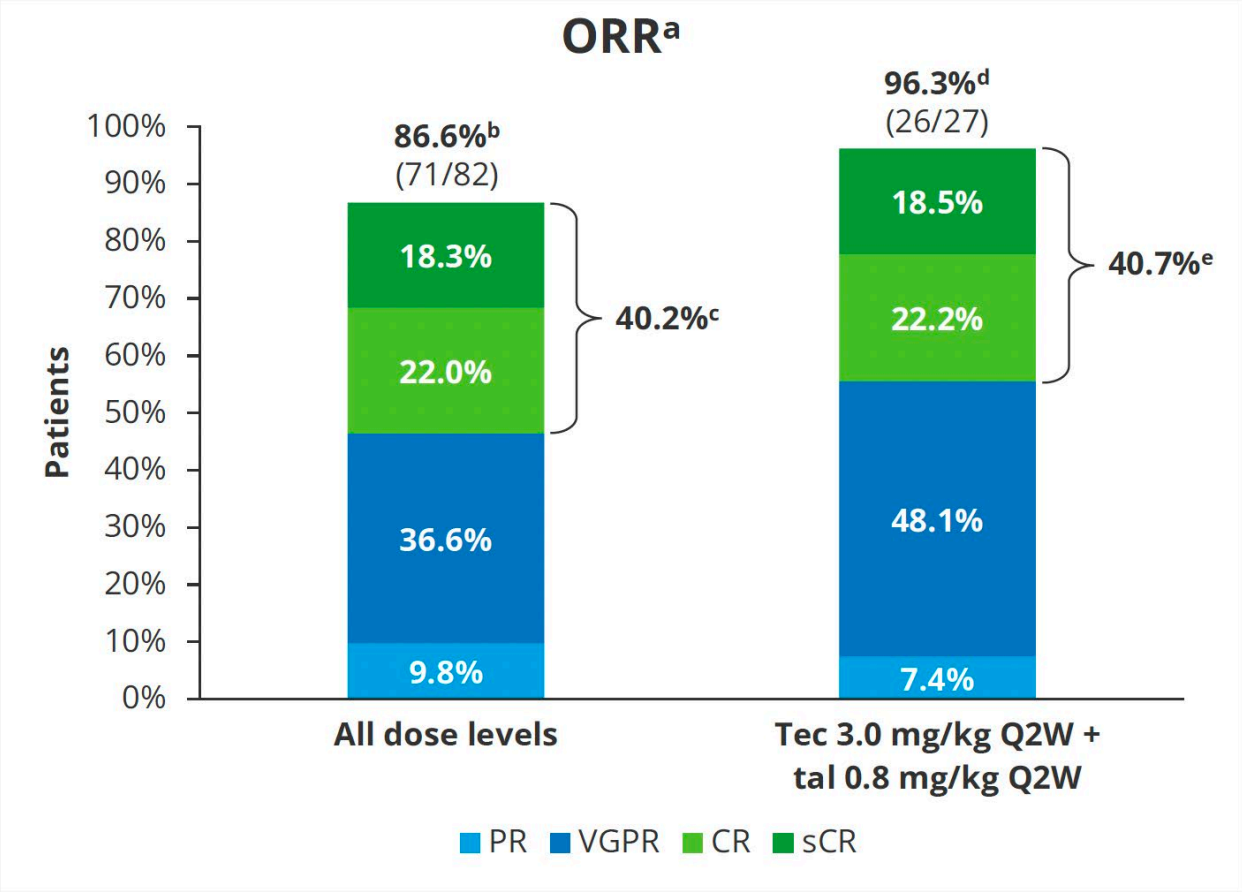
- **Teclistamab is the only approved BCMA×CD3 BsAb** with a personalized, weight-based, and flexible dosing schedule for the treatment of TCE RRMM[1]
  - ORR of 63% in MajesTEC-1[2]
- **Talquetamab is the most advanced GPRC5D-directed BsAb**, with promising efficacy in patients with RRMM[3]
  - ORR of >70% in MonumenTAL-1[3]
- Targeting 2 distinct antigens may overcome some resistance mechanisms to monotherapy[4]
- We report the first results from the phase 1b **RedirecTT-1** trial (NCT04586426) in patients with **RRMM**, **including a subset with EMD**



BCMA, B-cell maturation antigen; BsAb, bispecific antibody; EMD, extramedullary disease; GPRC5D, G protein–coupled receptor family C group 5 member D; ORR, overall response rate; RRMM, relapsed/refractory multiple myeloma; TCE, triple-class exposed. 1. TECVAYLI (teclistamab-cqyv). Prescribing information. Horsham, PA: Janssen Biotech, Inc; 2022. 2. Moreau P, et al. *New Engl J Med* 2022;387: 495-505. 3. Chari A, et al. *Blood* 2022;140 (suppl 1):384-7. 4. Fernandez de Larrea C, et al. *Blood* 2019;134 (suppl 1):136.

Mateos, et al. EHA 2023

RedirecTT-1: Efficacy



- ORR was high (86.6%) across all dose levels and 96.3% at the RP2R
- At data cut-off, 61% (57/93) of patients remained on treatment

	All dose levels (N=93)	Tec 3.0 mg/kg Q2W + tal 0.8 mg/kg Q2W (n=34)
Median follow-up, months (range)	13.4 (0.3–25.6)	8.1 (0.7–15.0)
Median DOR,[f] months (95% CI)	NE (NE–NE)	NE (NE–NE)
Median time to first response,[f] months (range)	1.97 (0–7.7)	1.48 (0–4.0)
Median time to best response,[f] months (range)	3.98 (1.1–15.7)	3.22 (1.4–10.7)
Median PFS,[g] months (95% CI)	20.9 (13.0–NE)	NE (9.9–NE)
9-month PFS rate[g] (95% CI)	70.1 (58.0–79.4)	77.1 (50.8–90.5)

Data cut-off date, March 16, 2023.
[a]Response was assessed by investigators, based on International Myeloma Working Group criteria; response-evaluable patients have received ≥1 study treatment and have ≥1 postbaseline response evaluation by investigator. [b]95% CI, 77.3–93.1%. [c]95% CI, 29.6–51.7%. [d]95% CI, 81.0–99.9%. [e]95% CI, 22.4–61.2%. [f]Includes patients with confirmed responses. [g]All treated patients. CR, complete response; DOR, duration of response; NE, not estimable; ORR, overall response rate; PFS, progression-free survival; PR, partial response; Q2W, every other week; RP2R, recommended phase 2 regimen; sCR, stringent complete response; VGPR, very good partial response.

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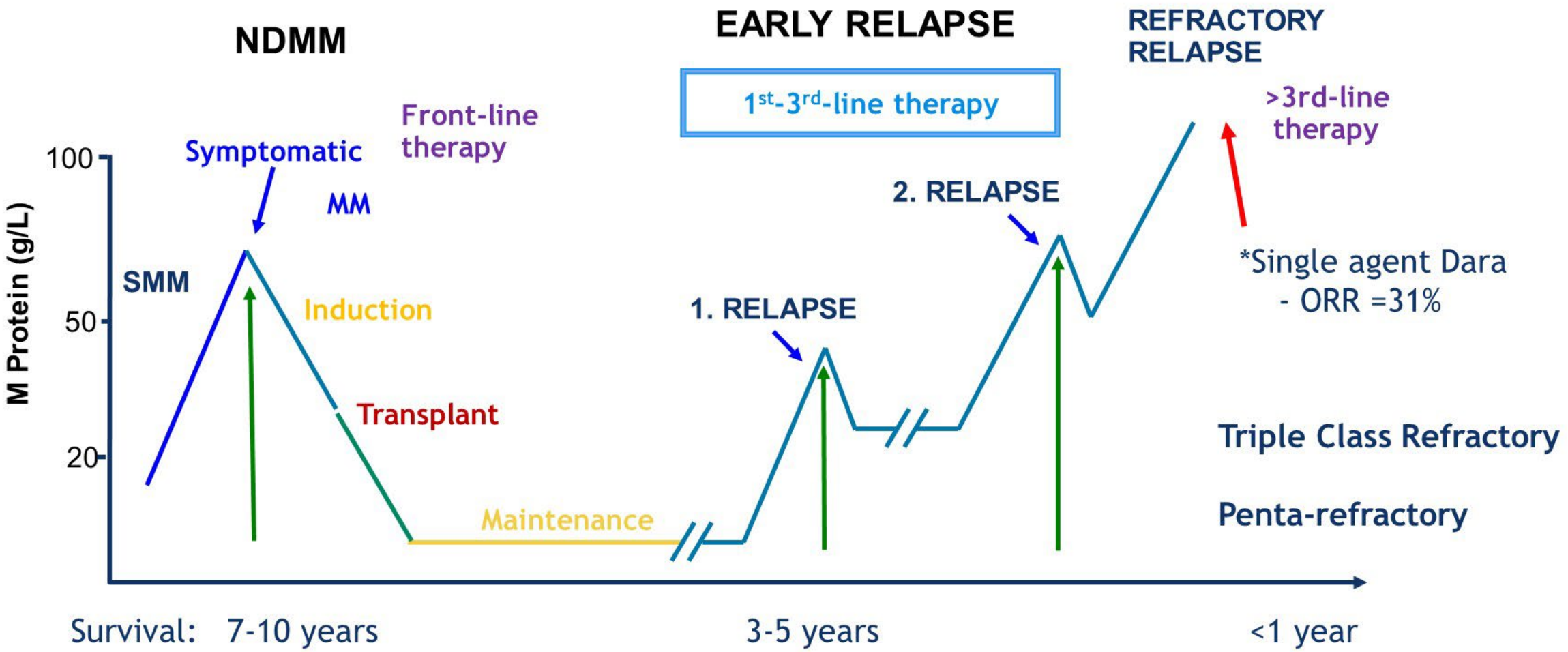
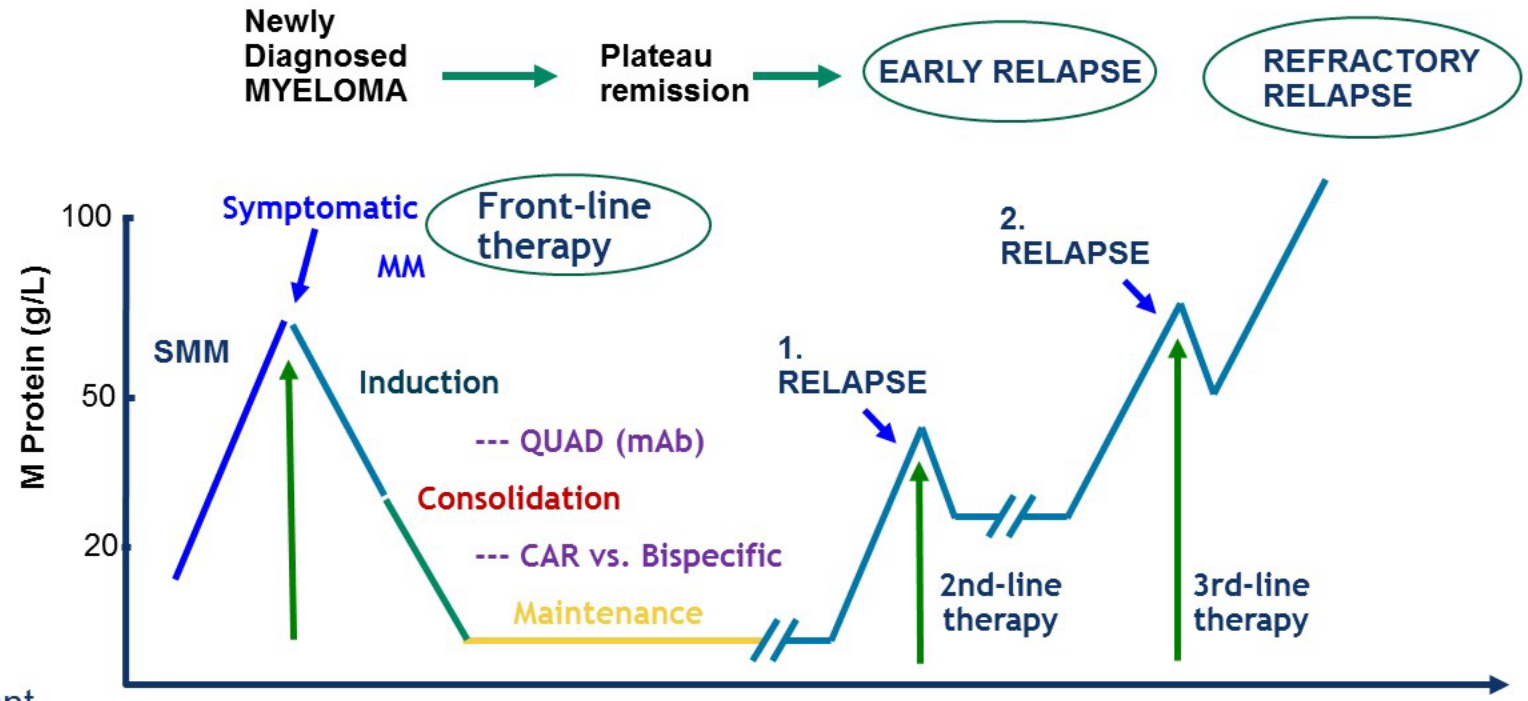
Natural History in Multiple Myeloma



Prediction: Future Strategies in MM (2025-2030)

Where and in what combination will immunotherapy have the most Impact?



SMM
Bispecific
- MRD x 6-12m
- STOP

Frontline
QUAD: No transplant

MRD (+): Consolidation: CAR (TE) vs. Bispecific (TI)
MRD (-): Maintenance: Len/mAb vs. Bispecific

Early Relapse (1-3 Prior Lines)
Novel CAR (Different Ag)
Novel Ab: ADC-combo vs. Bi-/Trivalent Ab

Late Relapse
Third party cellular therapy (NK + T)
Crispr strategies
Bispecific combinations

THANK YOU

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Mount Sinai
The Tisch Cancer Institute
Icahn School of Medicine at Mount Sinai

Q&A

oncology exchange

fall 2024

Clinical Session