Immune Therapy and Myeloma

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Options for Relapsed/Refractory Disease Continue to Increase

IMiDs	Proteasome inhibitors	Chemotherapy anthracyclines	Chemotherapy alkylators	Steroids	Other mechanisms of action	Monoclonal and bispecific antibodies	Cellular therapy
thalidomide	bortezomib	doxorubicin	cyclophosphamide	Dexamethasone	selinexor	elotuzumab	idecabtagene vicleucel
lenalidomide	carfilzomib	liposomal doxorubicin	Bendamustine	Prednisone	venetoclax	daratumumab	ciltacabtagene autoleucel
pomalidomide	ixazomib		Melphalan			isatuximab	
						teclistamab	
						talquetamab	
						elranatamab	

New formulations, new dosing, and new combinations, too!

What is Immune Therapy?

Immunotherapy

Passive/Active	Passive Immunity	Adjuvant Therapy	Active Therapy
Ab based T-cell	targeting a receptor	Immune Booster	Delivering Cells
T-Cell Engager	MoAB Direct Indirect	Dendritic cell or Peptide Vaccine	Allo Transplant, Car T-Cells
'Switzerland'	Truly 'Targeted' Therapy	'Connecting Flights'	Risk 'Off Target' effects

Who are the Players

1990's

IMIDS

Thal/Len/Pom

Celmods

Iberdomide

mezigdomide

2015

MoAbs

Daratumumab

Elotuzumab

Isatuximab

ADC

Belamaf

2020

CART

BCMA

Ide-cel

cilta-cel

GPRC5D

MCar

2022

TCE

BCMA

Teclistimab

Elranatamab

5 others

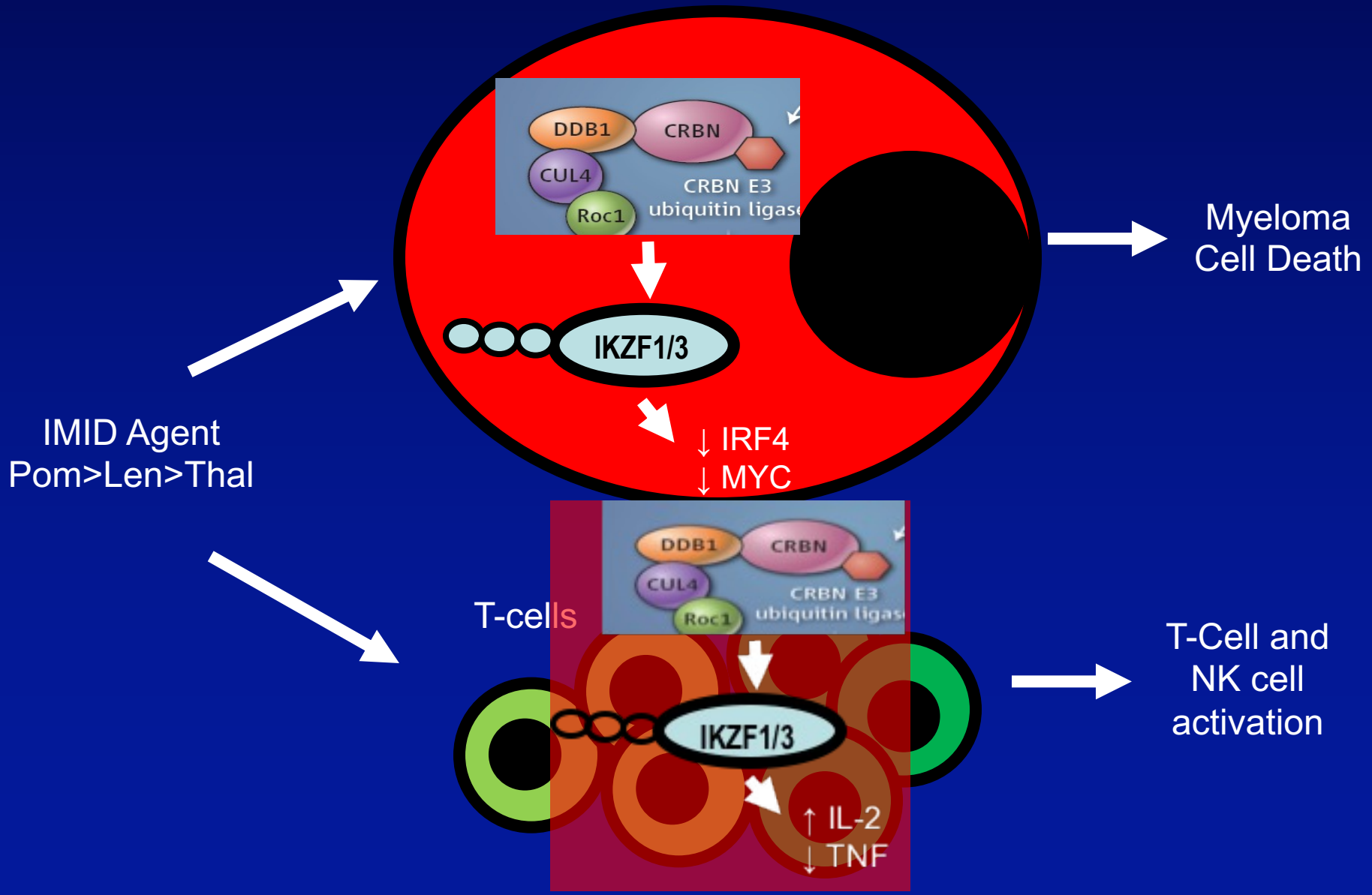
GPRC5D

Talquetamab

FCRH5

Cevostamab

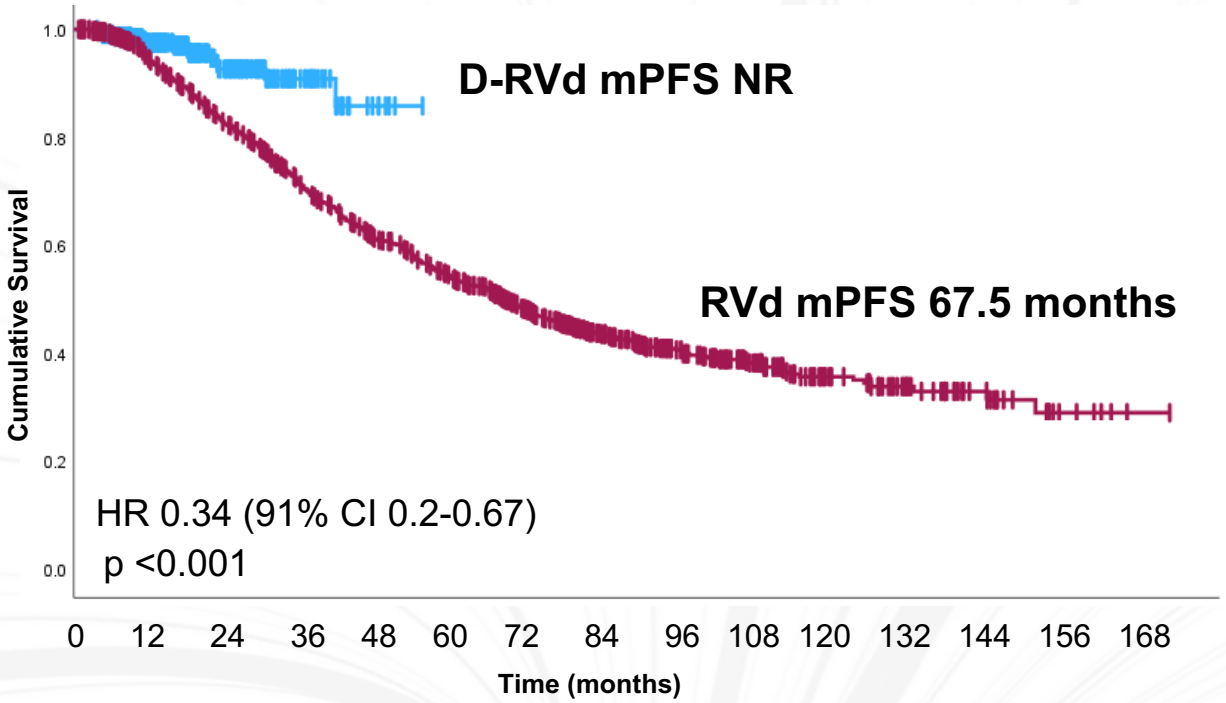
Differential Effects the Same Target



Joseph et al, ASH 2023

SURVIVAL OUTCOMES: OVERALL COHORT

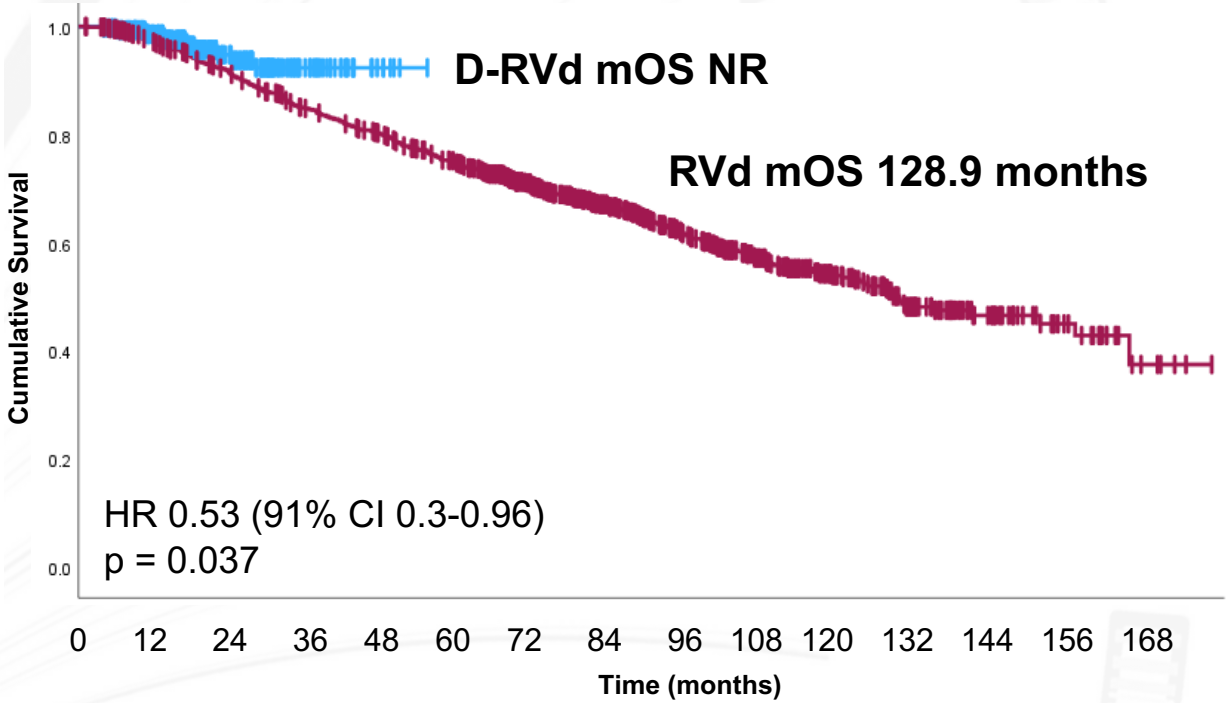
Progression Free Survival



1-year PFS, D-RVd vs RVd: 98% vs 93%
2-year PFS, D-RVd vs RVd: 93% vs 82%

Median follow up DRVd: 18 months, RVd: 87 months

Overall Survival



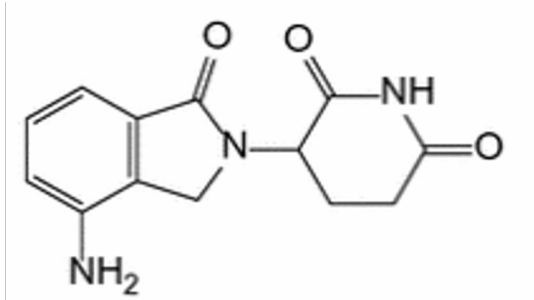
1-year OS, D-RVd vs RVd: 99% vs 97%
2-year OS, D-RVd vs RVd: 94% vs 91%

Median follow up DRVd: 18 months, RVD: 96 months

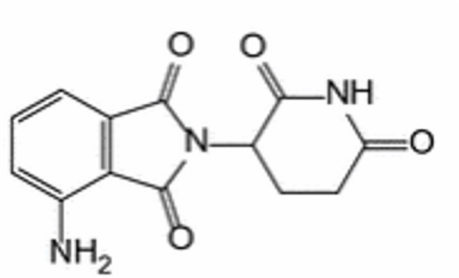
Novel cereblon E3 ligase modulators (CELMoD® agents) in development

LEN and **POM**
(a subgroup of CELMoD® agents)
helped to **transform therapy and drive survival** in MM[1-3]

LEN



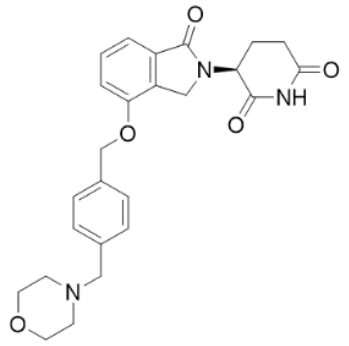
POM



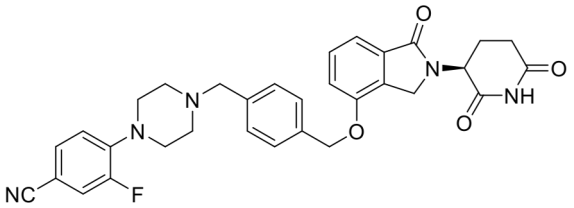
Rational selection of molecules based on **deep scientific understanding of CRBN and MM biology: iberdomide (IBER; CC-220) and mezigdomide (CC-92480)**[4-6]

2019 and 2020: First clinical data for IBER and CC-92480 in MM

IBER



CC-92480



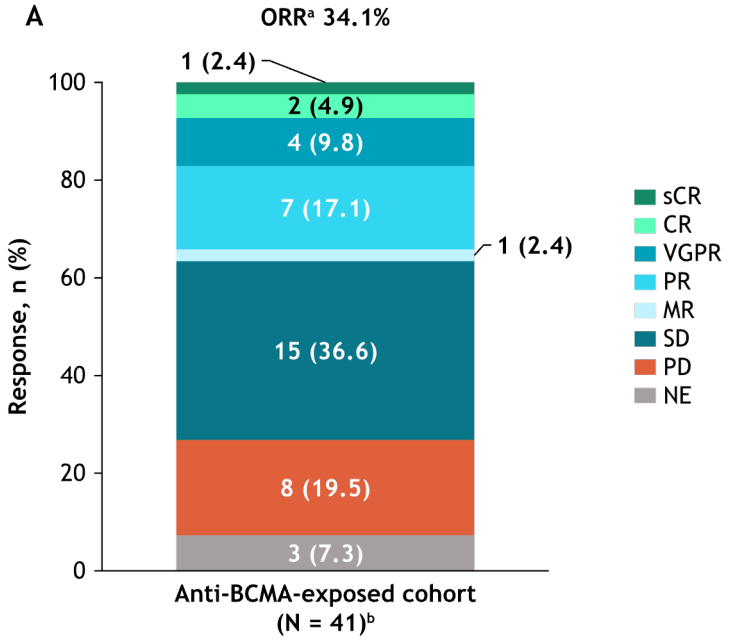
Iberdomide (IBER; CC-220) and mezigdomide (CC-92480) are investigational products, currently not approved by any regulatory agency.

CRBN, cereblon; IBER, iberdomide; LEN, lenalidomide; MM, multiple myeloma; POM, pomalidomide.

1. Rajkumar SV, et al. Lancet Oncol. 2010;11:29-37. 2. Facon T, et al. Blood. 2018;131:301-10. 3. Durie BGM, et al. Blood Cancer J. 2020;10:53. 4. Ito T, Handa H. Int J Hematol. 2016;104:293-9.
5. Matyskiela ME, et al. J Med Chem. 2018;61:535-42. 6. Hansen JD, et al. J Med Chem. 2020;63:6648-67.

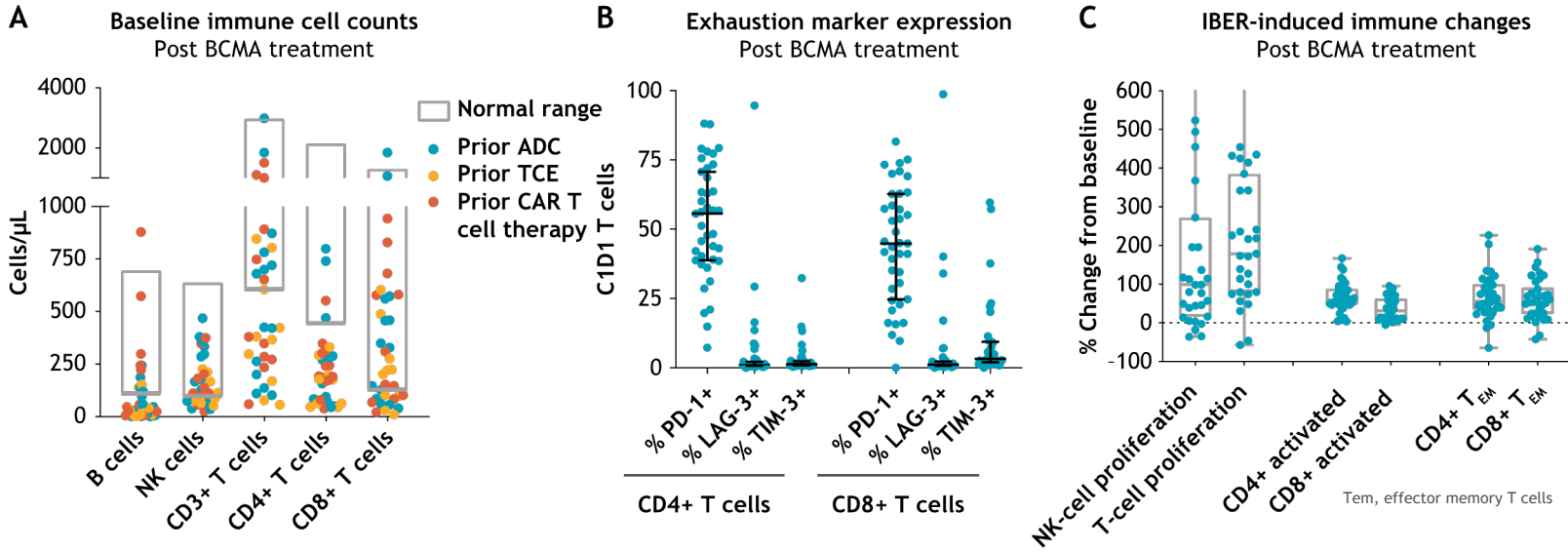
CC-220-MM-001 IBER+DEX (Cohort I) efficacy and safety in patients with heavily pretreated, anti-BCMA-exposed RRMM

Efficacy (ORR) and safety of IBER+DEX in anti-BCMA-exposed patients with RRMM



[a]PR or better; [b]Data cutoff: August 1, 2022; [c]Includes viral pneumonia, bacterial pneumonia, COVID-19 pneumonia, *Pneumocystis jirovecii* pneumonia, and pseudomonal pneumonia.
COVID-19, coronavirus disease 2019; MR, minimal response; NE, not evaluable; SD, stable disease; TEAE, treatment-emergent adverse event.

IBER is immune-stimulatory post-BCMA therapy

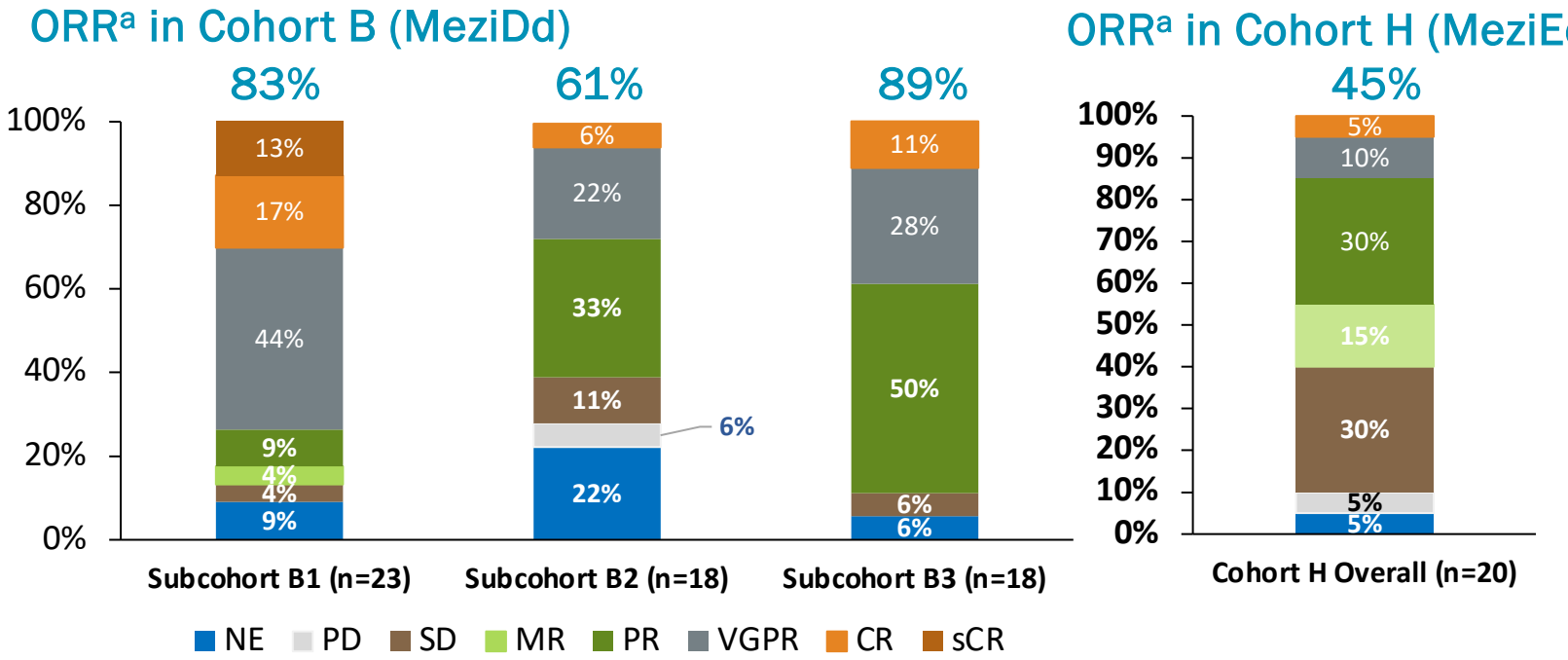


Most frequent (≥ 20% all grade) TEAEs and events of interest,[b] n (%)	Anti-BCMA-exposed cohort IBER + DEX (N = 41)		
	All grades	Grade 3	Grade 4
Hematologic TEAEs			
Neutropenia	23 (56.1)	11 (26.8)	10 (24.4)
Febrile neutropenia	1 (2.4)	1 (2.4)	0
Anemia	15 (36.6)	11 (26.8)	0
Thrombocytopenia	12 (29.3)	4 (9.8)	4 (9.8)
Leukopenia	12 (29.3)	6 (14.6)	4 (9.8)
Lymphopenia	9 (22.0)	2 (4.9)	6 (14.6)
Non-hematologic TEAEs			
Fatigue	15 (36.6)	2 (4.9)	0
Diarrhea	10 (24.4)	1 (2.4)	0
Constipation	10 (24.4)	0	0

[a]PR or better; [b]Data cutoff: August 1, 2022; [c]Includes viral pneumonia, bacterial pneumonia, COVID-19 pneumonia, *Pneumocystis jirovecii* pneumonia, and pseudomonal pneumonia.
COVID-19, coronavirus disease 2019; MR, minimal response; NE, not evaluable; SD, stable disease; TEAE, treatment-emergent adverse event.

Lonial S, et al. ASH 2022; CC-220-MM-001 Study

Results From the Phase 1/2 Study of Mezigdomide + Dex and Dara or Elo in RRMM: Efficacy

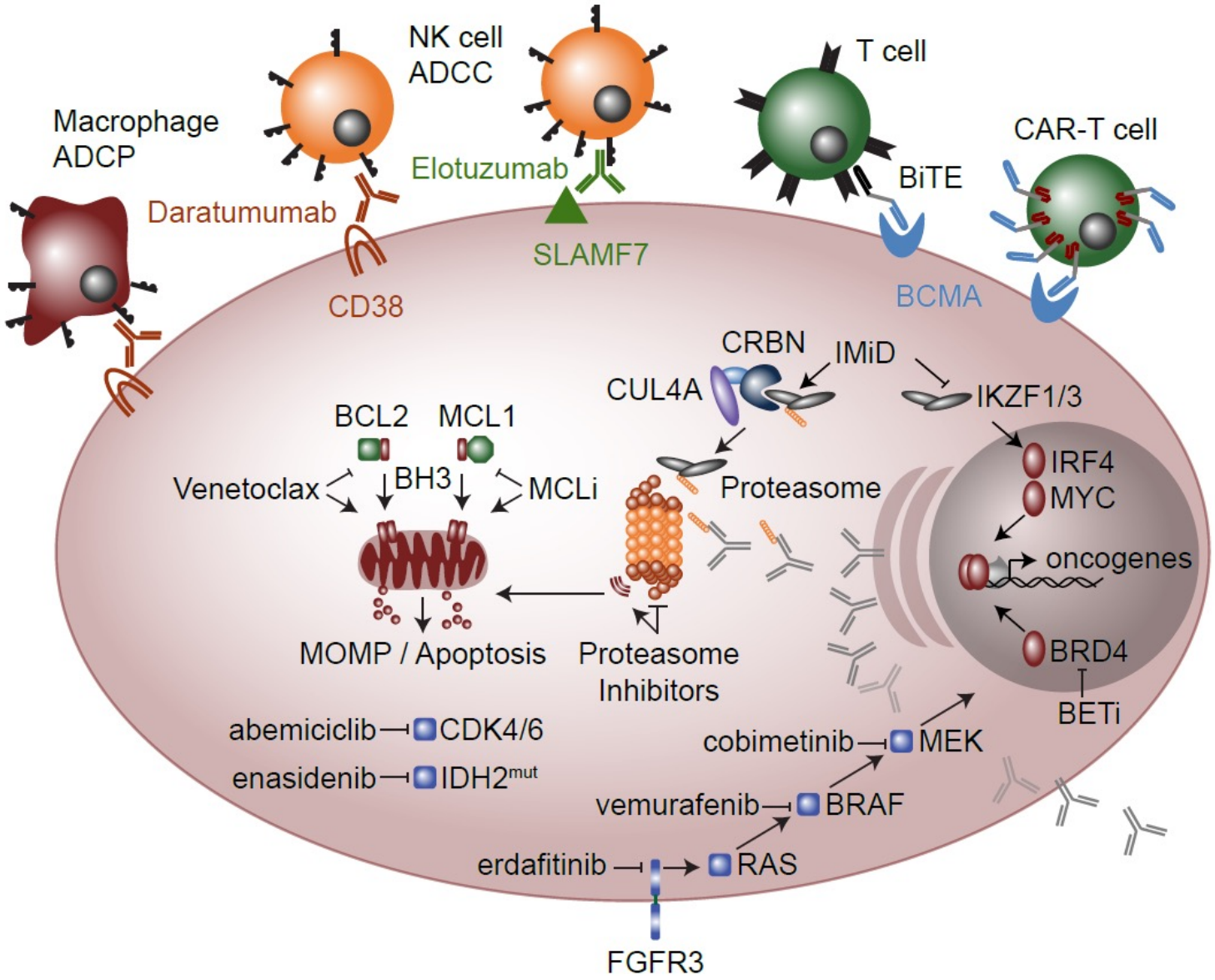


- Combined ORR for cohort B (MeziDd) was 78%
- Lower ORR to date in Subcohort B2 might be explained by the median follow-up time of only 3 mo
- Among the efficacy-evaluable population in Subcohort B2, only 1 PD was reported
- Importantly, dose exposure per cycle was highest in patients receiving Mezi for 3 out of 4 weeks and lowest in patients receiving Mezi for 1 out of 2 weeks, suggesting that Subcohort B2 is not yet mature for ORR

	Cohort B (MeziDd)			Cohort H (MeziEd)
	Subcohort B1	Subcohort B2	Subcohort B3	
Median time to first response[b] (range), mo	1.18 (0.9-4.6)	0.89 (0.7-2.8)	1.61 (0.9-4.6)	0.95 (0.9-2.8)
Median DOR (95% CI), mo	NR (23.3-NR)	NR (4.6-NR)	9.5 (9.5-NR)	5.0 (3.7-NR)
Median follow-up[c] (range), mo	22.6 (0.7-39.6)	3.1 (0.5-15.2)	6.6 (2.8-14.1)	7.1 (2.0-21.7)

[a]PR or better. [b]Data derived from the safety population. [c]Data derived from the full analysis population.
Data cut-off: July 6, 2023
Richardson P, et al. ASH 2023. Abstract 1013.

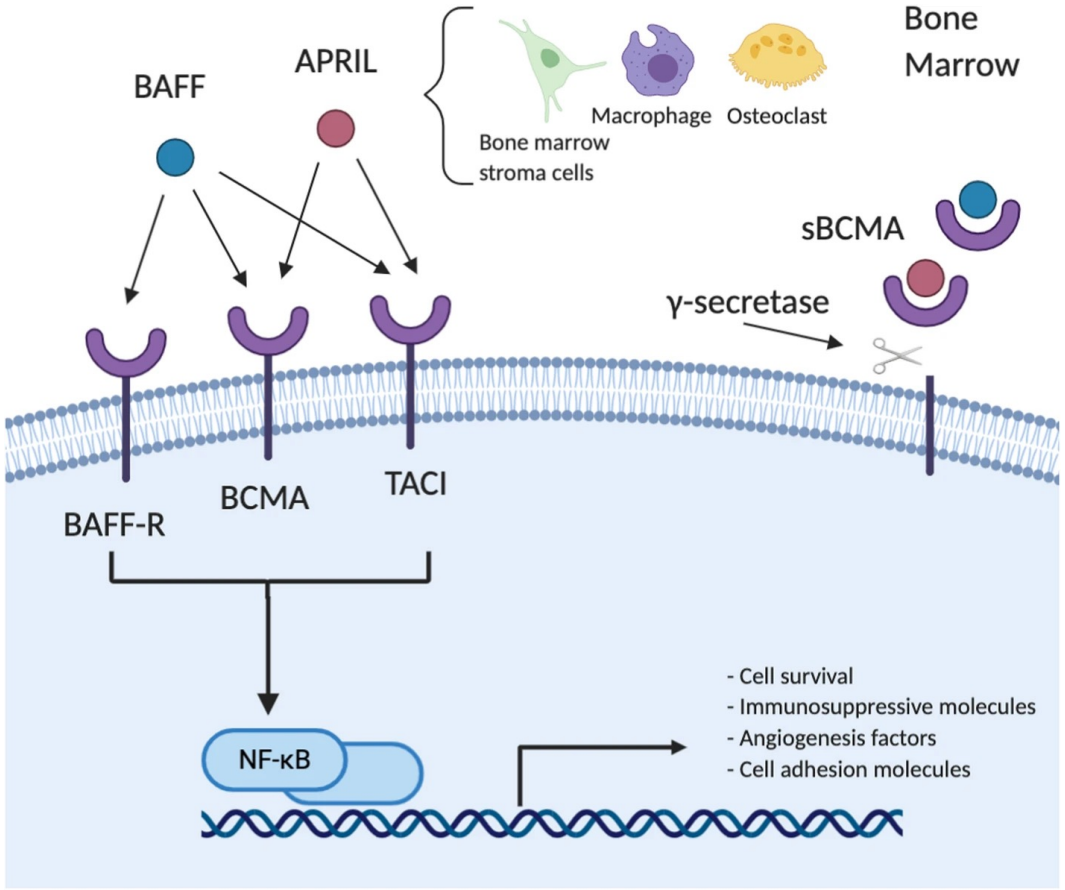
Therapeutic modalities in multiple myeloma



Barwick et al.
Frontiers Immunology, 2019

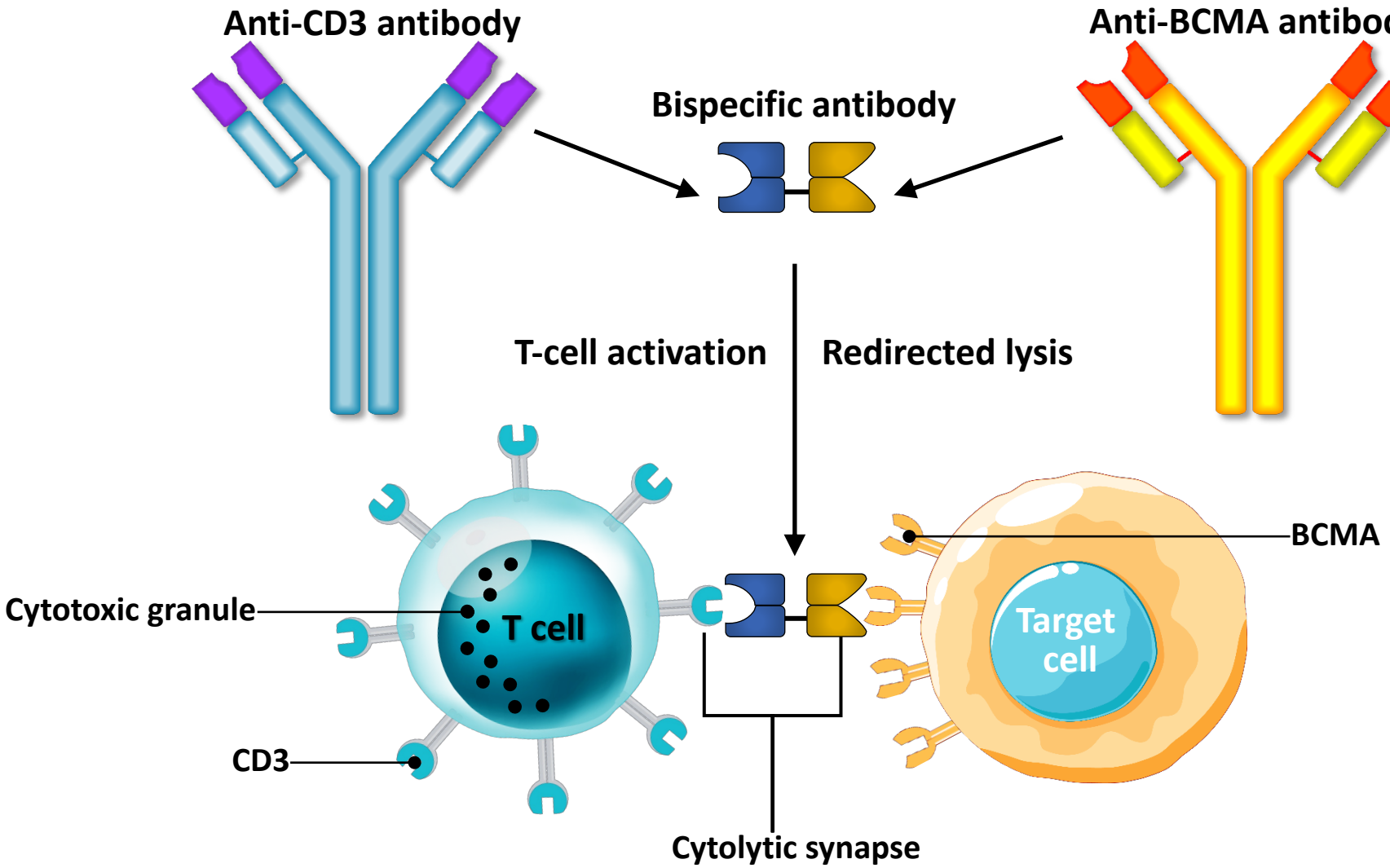
BCMA: Expression on Plasma Calls

- Expressed
  - on surface of nearly all MM cell lines
  - in malignant PCs > in normal PCs
- ↑ BCMA levels are associated with ↓ outcomes
- Upregulated expression during MM pathogenesis and evolution (normal → MGUS → SMM → active MM)



Yu B, et al. *J Hematol Oncol*. 2020;13:125.

Bispecific T Cell Engagers



Baeuerle PA, et al. *Cancer Res*. 2009;69:4941-4944.

BCMAxCD3 Bispecifics

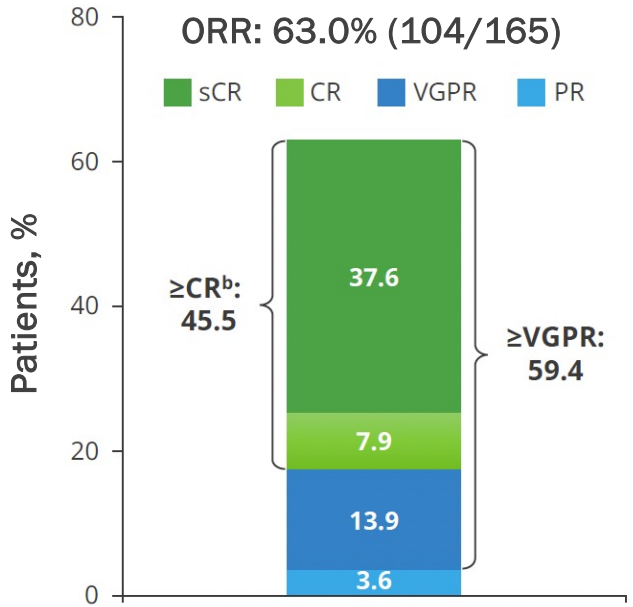
Bispecific Antibody	Teclistamab[1-2] (JNJ-64007957)	Elranatamab[3] (PF-06863135)	Linvoseltamab[4] (REGN5458)	ABBV-383[5-6]	Alnuctamab[7] BMS-93269	HPN217[8]
Structure/Function	Humanized antibody	Humanized antibody	*Veloci-Bi*® platform fully human antibody	Low CD3 affinity fully human antibody	Humanize antibody 2 BCMA + 1 CD3	Trispecific 50kDa (albumin)
Treatment	Weekly SC	Weekly SC	Weekly IV	IV q3w	Qwk -> Q4wk SQ	Q2wk IV
Patients	n= 165	n= 123	n= 252	n= 174	n= 68	n= 62
Median prior lines	5	5	5	5	4	6
Triple-class refractory	78%	97%	81%	80%	63%	76%
ORR at RP2d	63%	61%	64%	58-61%	65%	73%
RP2D (n)	1.5 mg/kg SC **(n=165)**	76 mg SQ **(n=123)**	200 mg IV (n=58)	40 to 60 mg IV (n=52 n=59)	30 mg SQ (n=26)	?12 or 24 mg (n=13)
PFS	11.3 mos (8.8-17.1)	NE @ 12 mos	NR	13.7 or 11.2 mos	NR	NR
DOR	18.4 mos (14.9-NE)	NE @12 mos	89% @ 6 mos	NE	NE	NR
Median f/u	14.1 mos /23 mos	10.4 mos	3.2 mos	6.8	4.6 mos	
AEs, (All/(Gr 3+);						
CRS	72% (0.6%)	58% (0%)	44% (1%)	60% (1%)	53% (0%)	27 (0%)
Infections	80% (55%)	67% (35%)	54% (29%)	(22%)	34% (9%)	45% (16%)
Neutropenia	72% (66%)	48% (48%)	25% (23%)	34% (26%)	37%(32%)	16% (13%)
Anemia	52% (37%)	48% (37%)	36% (31%)	37% (16%)	38%(25%)	44% (34%)
Thrombocytopenia	40% (21%)	26% (24%)	18% (6%)	29% (11%)	24%(9%)	NR
Neuro	Neurotoxicity 15% (0.1)	NR/ PN?	ICANS 2% (1%)	5% (0.1%)	ICANS 3 (0%)	16% (0%)
# Deaths	68/(41 due to PD)	21 (/11 due to PD)	NR	46	1	NR
Hypogamma/IVIg	72%//46%	75%/40%	NR	NR		

Accelerated approval

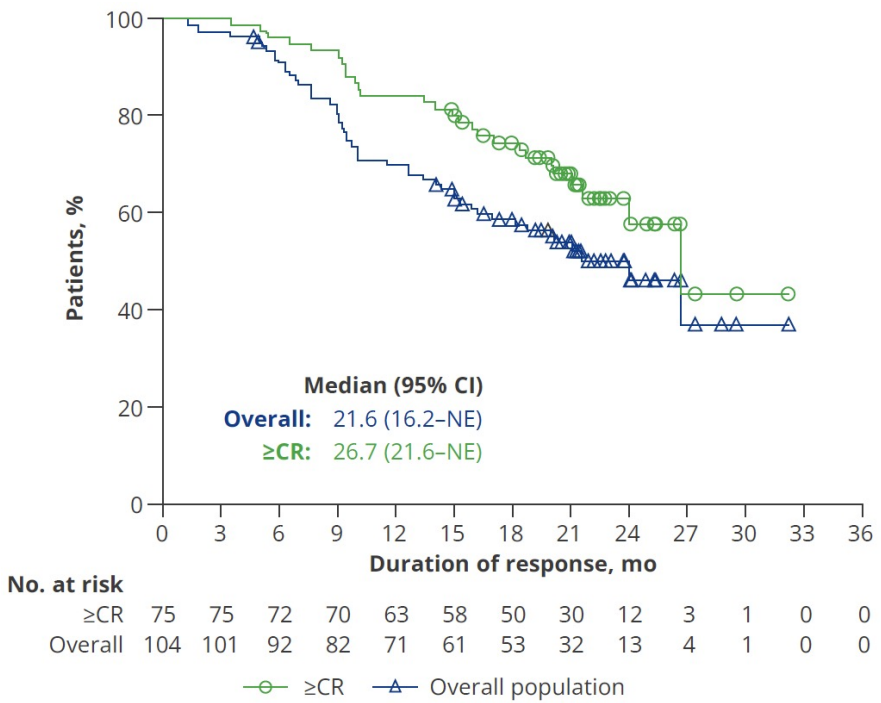
1. Moreau P, et al. *N Engl J Med.* 2022;387:495-505. 2. Van de Donk N, IMS 2023; Abstract OA-51. 3. Lesohkin AM, et al. *Nature Med.* 2023;29:2259-2267. 4. Bumma N, et al. *Blood.* 2022;140(Suppl 1):10140-10141. 5. Voorhees PM, et al. *Blood.* 2022;140(Suppl 1):4401-4404. 6. D'Souza A, et al. J Clin Oncol. 2022;40(31):3576-3586. 7. Wong SW, et al. *Blood.* 2022;140(Suppl. 1):400-402. 8. Abdallah AO, et al. *Blood.* 2022;140(Suppl 1):7284-7285.
Courtesy of A. Chiari.

Long-Term Follow-Up Results From the MajesTEC-1 Phase 1/2 Study of Teclistamab in Patients With RRMM: Treatment and Response

Best Response



DOR



Additional Response Data

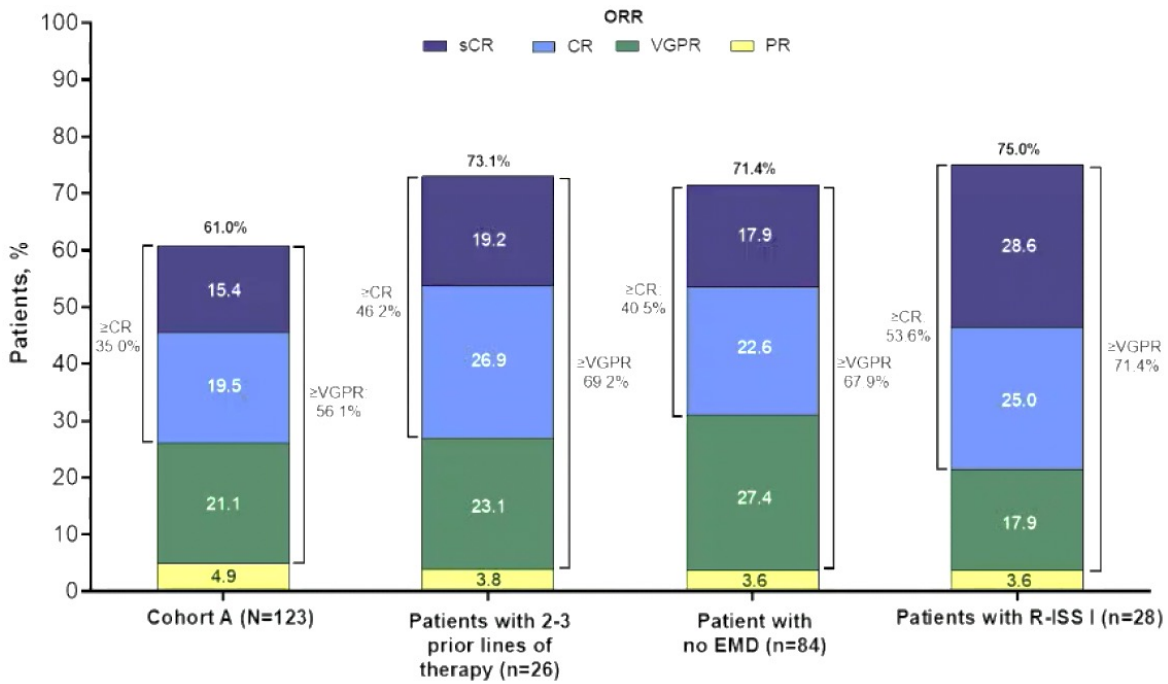
- ORR was consistent across clinically relevant subgroups
  - ≤3 prior LOT: 74.4% (32/43)
  - >3 prior LOT: 59.0% (72/122)
  - High-risk cytogenetics and/or EMD: 53.3% (32/60)
- Median time to first response: 1.2 months (range, 0.2-5.5)
- Median time to ≥CR: 4.6 months (range, 1.6-18.5)
- Median DOR increased since the previous report
- 34/42 (81.0%) MRD-evaluable patients (at day 100) were MRD negative (10^{-5})
  - 44/54 (81.5%) MRD-evaluable patients (as of March 2022) were MRD negative at any point

- At median follow-up of 23 months (data cutoff: January 4, 2023)
  - 165 patients had received RP2D of teclistamab
  - 47 patients remained on treatment; 42 had switched to q2w dosing (9 on q4w)
    - 41 of these patients maintained a deep response

van de Donk NWCJ, et al. ASCO 2023. Abstract 8011.

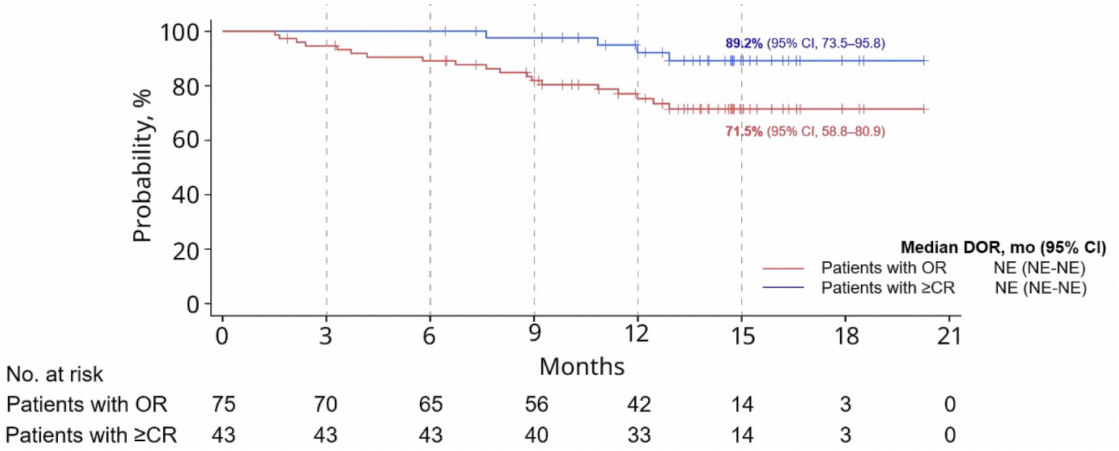
Updated Cohort A Results From the MagnetisMM-3 Phase 2 Study of Elranatamab in BCMA-Naive Patients With RRMM: Response

ORR by BICR



- Confirmed ORR by BICR: 61.0% (95% CI, 51.8-69.6)
  Median time to response: 1.2 months (range, 0.9-7.4)
- MRD negativity (10^{-5}): 89.7% of evaluable patients who achieved CR/sCR (n=29)

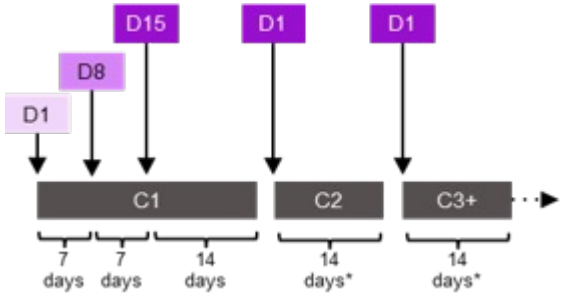
DOR by BICR (Responders Only)

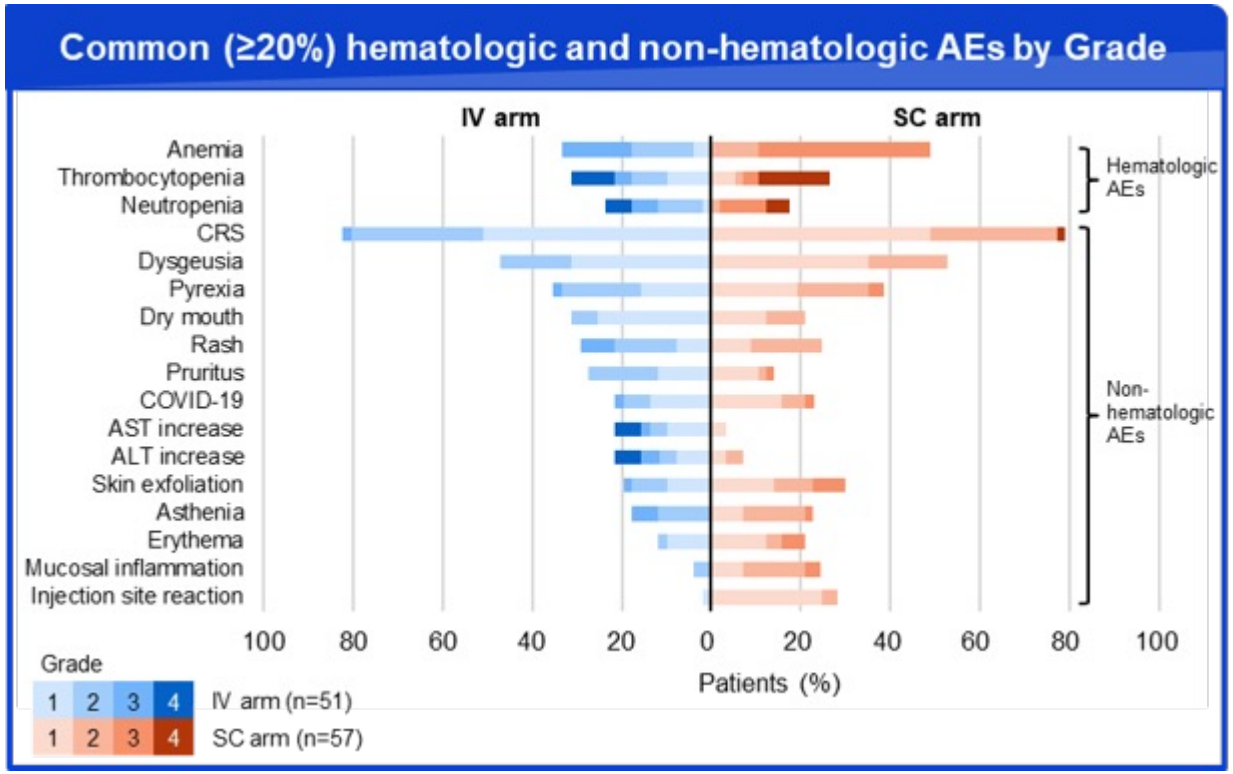


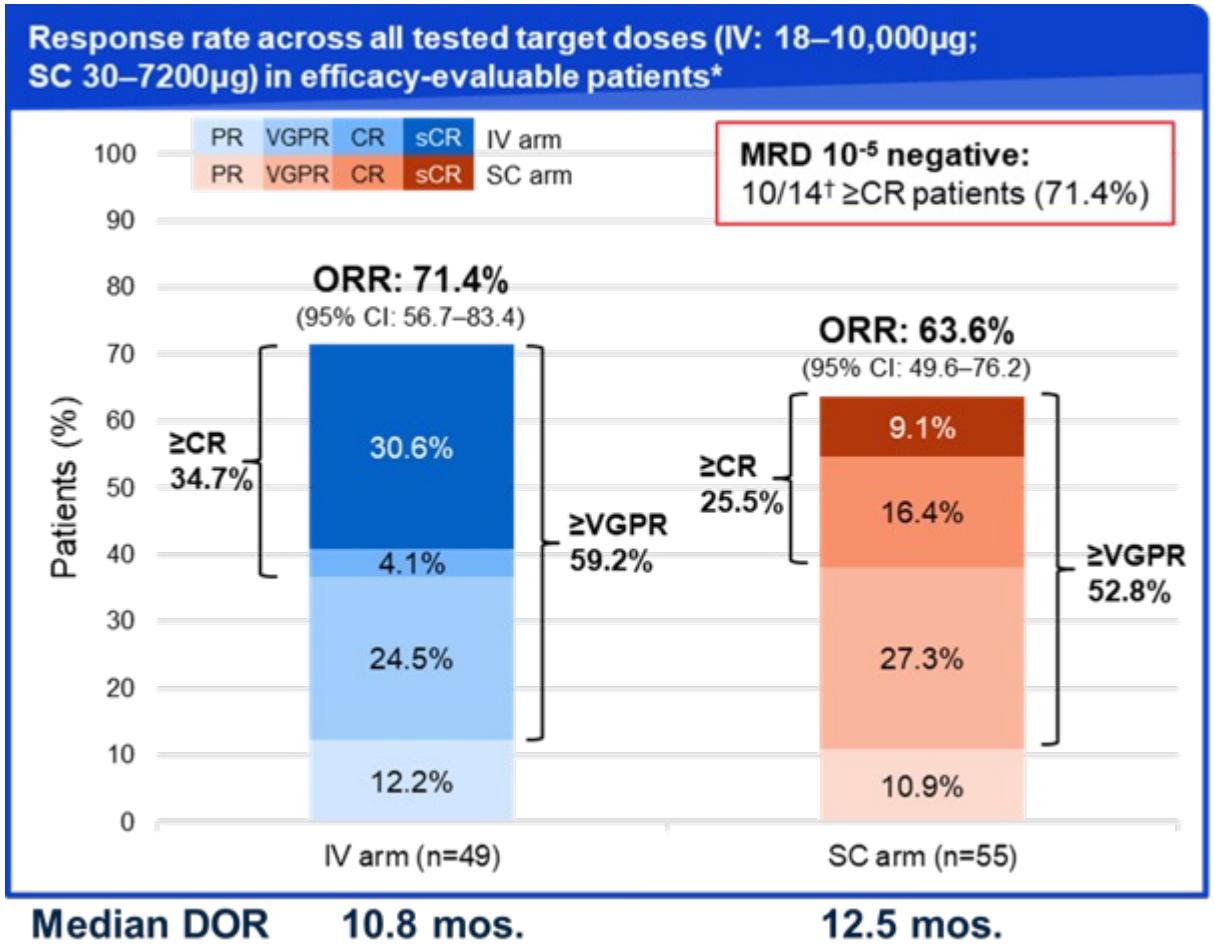
- 50 patients had a response per BICR and switched to q2w dosing
  - 40 of these patients (80%) maintained or improved their response ≥6 months after the switch
- 66.7% (50/75) objective responses were ongoing

Mohty M, et al. EHA 2023. Abstract S196.

Forimtamig: *GPRC5D x CD3 bsAb*

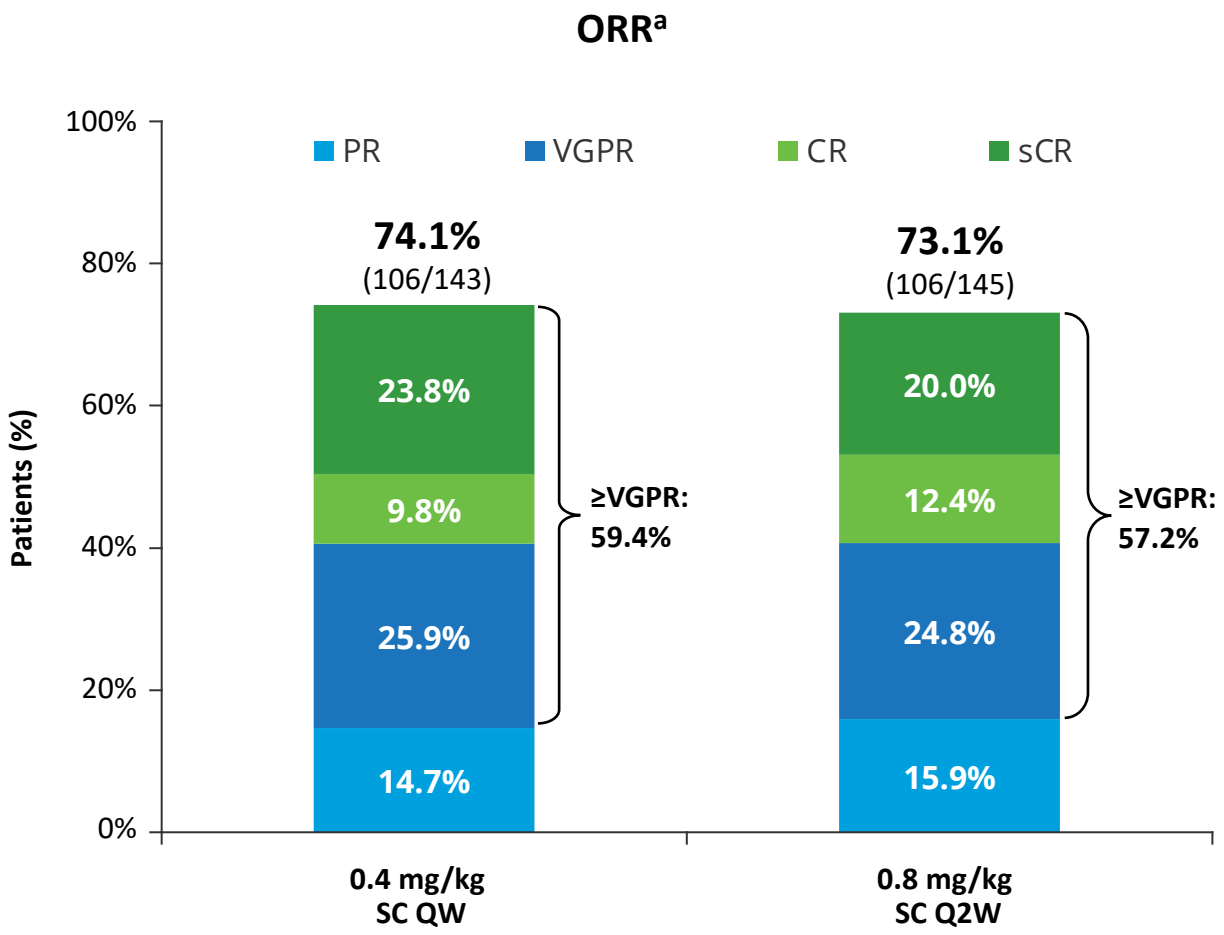






Carlo-Stella et al, ASH 2022

MonumenTAL-1: *ORR was similar for QW and Q2W schedules, and in triple and penta-refractory patients*



- **Triple-class refractory: 72.6%** (95% CI, 63.1–80.9) and **71.0%** (95% CI, 61.1–79.6)
- **Penta-drug refractory: 71.4%** (95% CI, 55.4–84.3) and **70.6%** (95% CI, 52.5–84.9)
- ORR was consistent across subgroups including baseline ISS stage III disease, baseline cytogenetic risk, number of prior therapies, refractoriness to prior therapy, and belantamab exposure, except among patients with baseline plasmacytomas

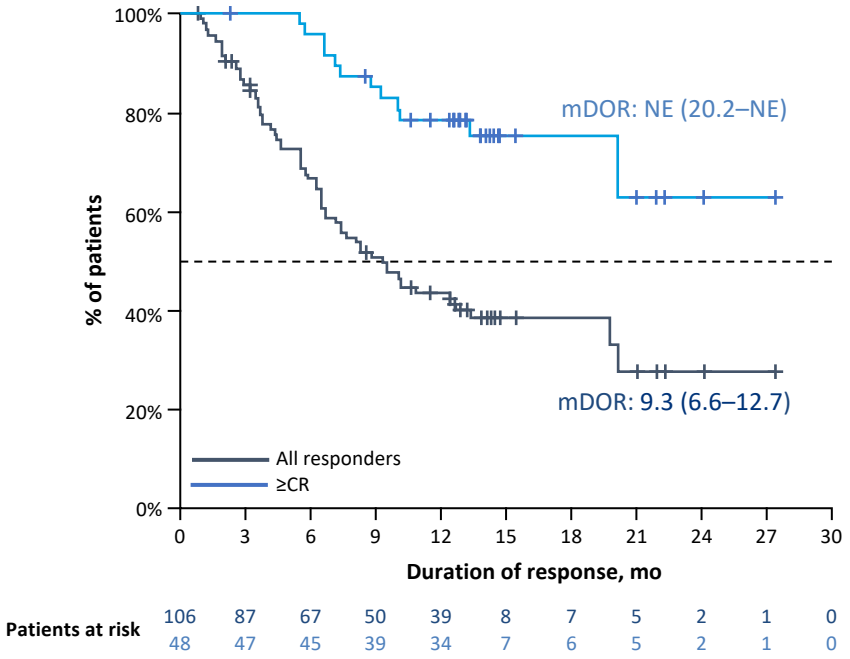
Timing, months	0.4 mg/kg SC QW n=143	0.8 mg/kg SC Q2W n=145
Median (range) follow-up, efficacy	14.9 (0.5[b]–29.0)	8.6 (0.2[b]–22.5)
Median (range) time to first response[c]	1.2 (0.2–10.9)	1.3 (0.2–9.2)
Median (range) time to best response[c]	2.2 (0.8–12.7)	2.7 (0.3–12.5)

Chari et al., ASH 2022

MonumenTAL-1: *Treatment at both doses led to durable responses*

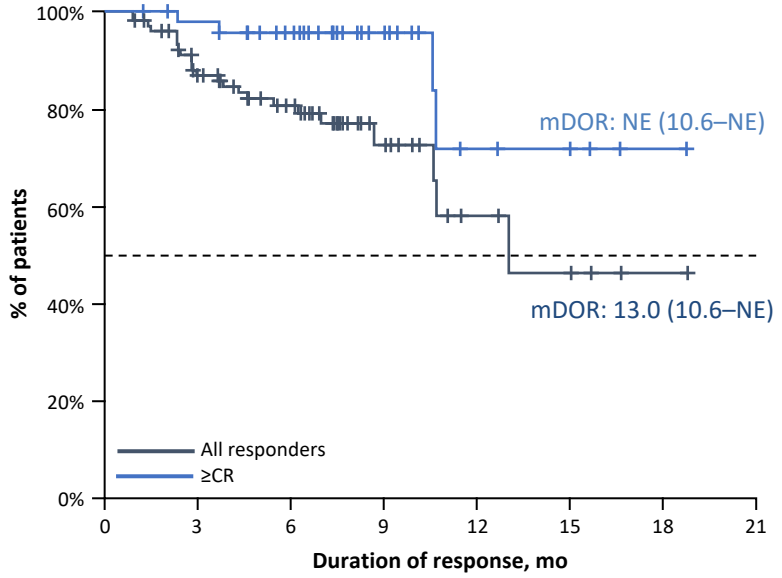
Median DOR not reached for those patients who achieved ≥CR

DOR, 0.4 mg/kg SC QW[a]



Patients at risk											
	106	87	67	50	39	8	7	5	2	1	0
	48	47	45	39	34	7	6	5	2	1	0

DOR, 0.8 mg/kg SC Q2W[b]



Patients at risk								
106	82	51	16	6	4	1	0
47	44	32	14	5	4	1	0

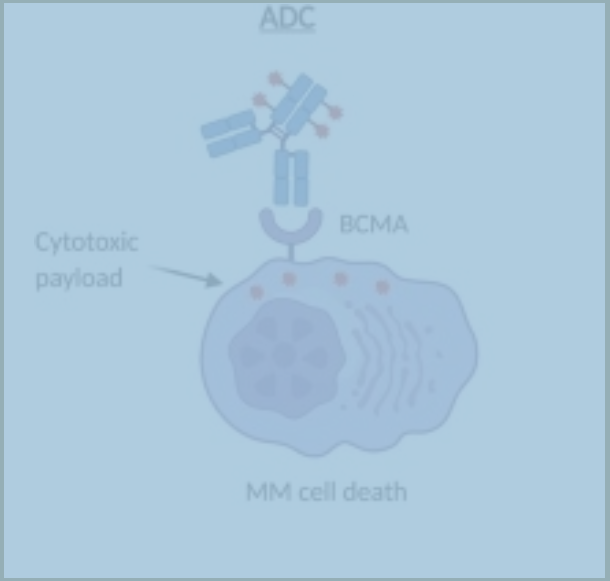
mPFS: 7.5 months (95% CI: 5.7–9.4; 33% censored)

11.9 months (95% CI: 8.4–NE; 61% censored)

Chari et al., ASH 2022

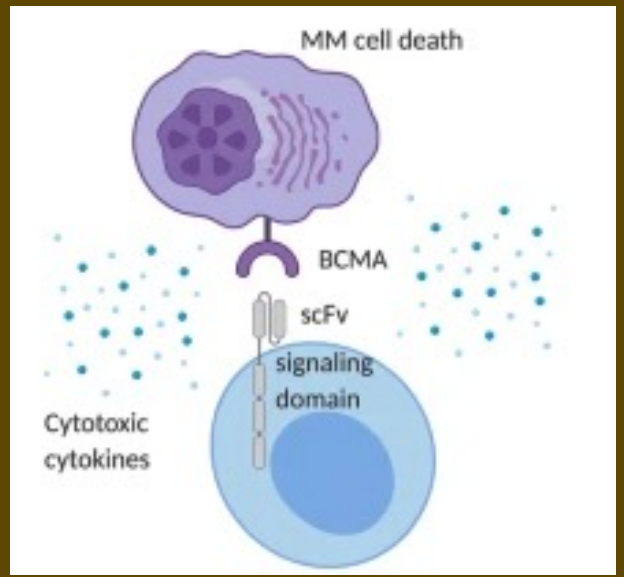
Targeted Therapy for RRMM

ADC[1]



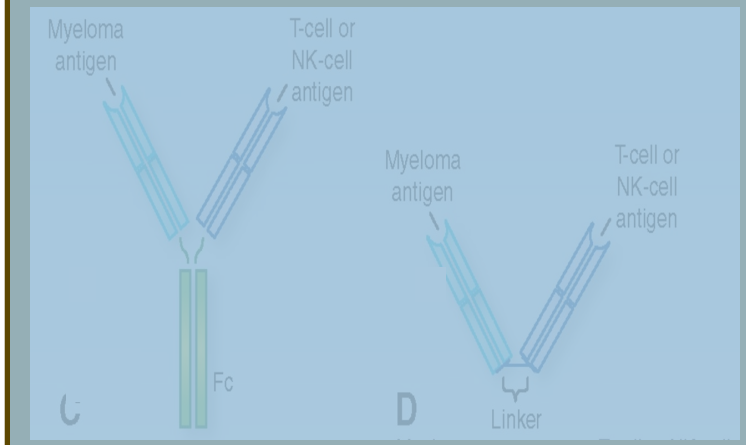
- ADC binds to BCMA on MM cell surface and is internalized
- Linker hydrolysis inside of lysosomes/endosomes
- Cytotoxic payload released to induce cell death.

CAR T[2]



- **Ectodomain of BCMA scFv on CAR T cells binds to BCMA on MM cell surface**
- **Leads to:**
  - **CAR T-cell activation, cytotoxic cytokine release, and MM cell death**

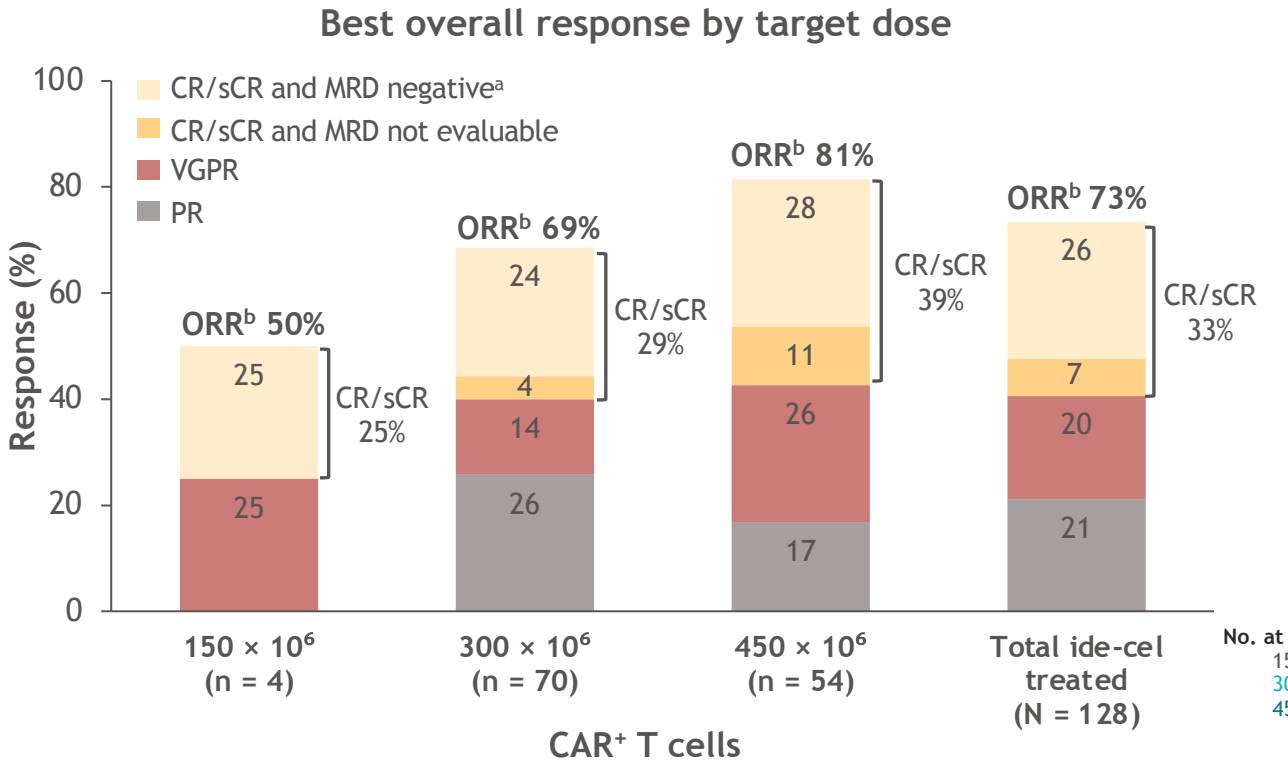
Bispecific Ab[2]

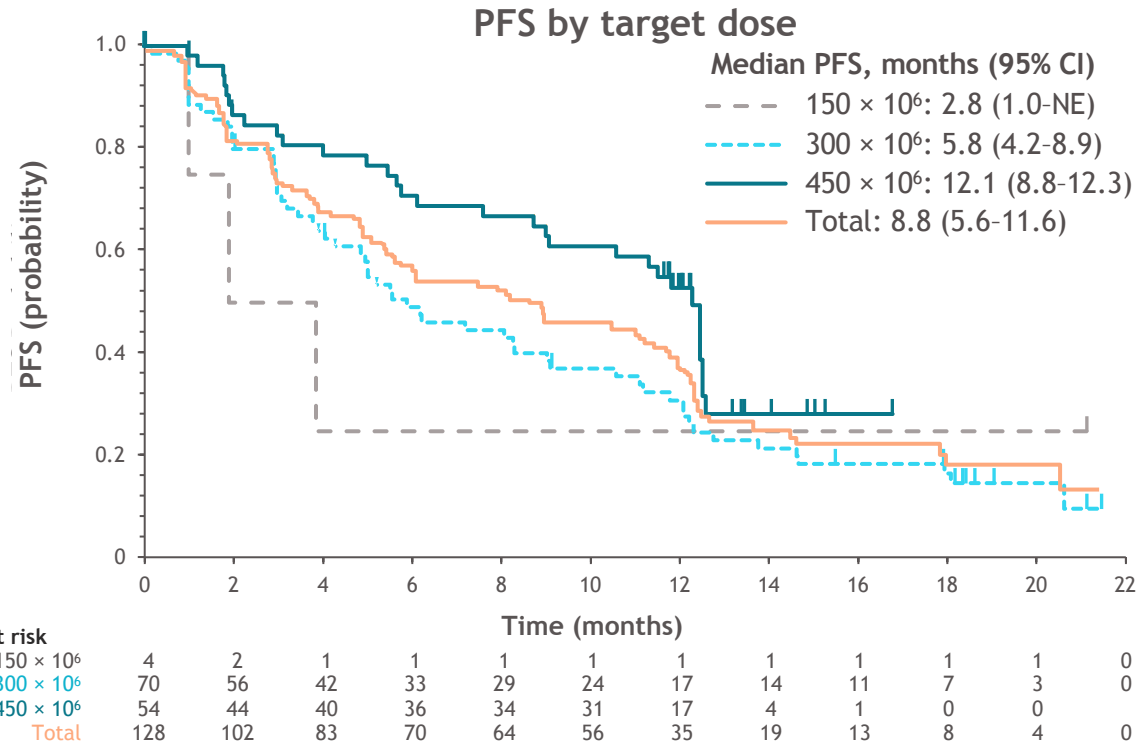


- Bispecific antibodies bind both a target on malignant plasma cells and on cytotoxic immune effector cells [T cells/NK cells] to create an immunologic synapse; leads to:
  - T/NK-cell activation and destruction of malignant plasma cells

1. Yu B, et al. *J Hematol Oncol*. 2020;13:125.
2. Lancman G, et al. *Blood Cancer Discov*. 2021;2:423-433.

Ide-cel delivers high response rates and PFS in RRMM





Median follow-up: 13.3 months across target dose levels

PFS increased with higher target dose

Data cut-off date: 14 January 2020. Values may not add up due to rounding.

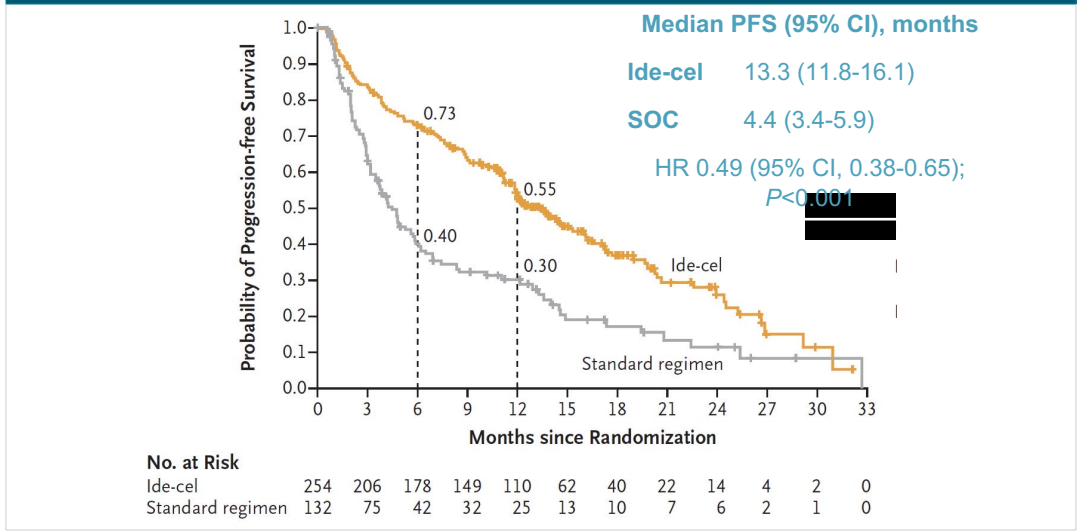
[a] MRD negative defined as < 10^{-5} nucleated cells by next-generation sequencing; only MRD values within 3 months of achieving CR/sCR until PD/death (exclusive) were considered. [b] Defined as ≥ PR.
CR, complete response; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

Munshi NC, et al. N Eng J Med. 2021;384:705-16.

KarMMA-3: Ide-Cel in Earlier Lines of Therapy in RRMM

Efficacy and Safety[1,2]

PFS



Response, n (%)	Ide-Cel (n=254)	SOC (n=132)
ORR[a]	181 (71)	55 (42)
CR/sCR	98 (39)	7 (5)
VGPR	55 (22)	13 (10)
PR	28 (11)	35 (27)
SD	31 (12)	48 (36)
PD	24 (9)	10 (8)

AEs	Ide-Cel (n=250)		SOC (n=126)	
(≥25% Any Grade)	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Nonhematologic				
CRS[b]	197 (88)	9 (4)	0	0
Infection[c]	146 (58)	61 (24)	68 (54)	23 (18)
Nausea	112 (45)	4 (2)	34 (27)	0
Diarrhea	85 (34)	4 (2)	30 (24)	4 (3)
Hypophosphatemia	78 (31)	50 (20)	10 (8)	3 (2)
Hypokalemia	78 (31)	12 (5)	14 (11)	1 (1)
Fatigue	69 (28)	4 (2)	44 (35)	3 (2)
Pyrexia	69 (28)	2 (1)	22 (17)	1 (1)
Constipation	67 (27)	0	9 (7)	0
Hematologic				
Neutropenia	195 (78)	189 (76)	55 (44)	50 (40)
Anemia	165 (66)	127 (51)	45 (36)	23 (18)
Thrombocytopenia	136 (54)	106 (42)	36 (29)	22 (17)
Lymphopenia	73 (29)	70 (28)	25 (20)	23 (18)
Leukopenia	72 (29)	71 (28)	15 (12)	11 (9)

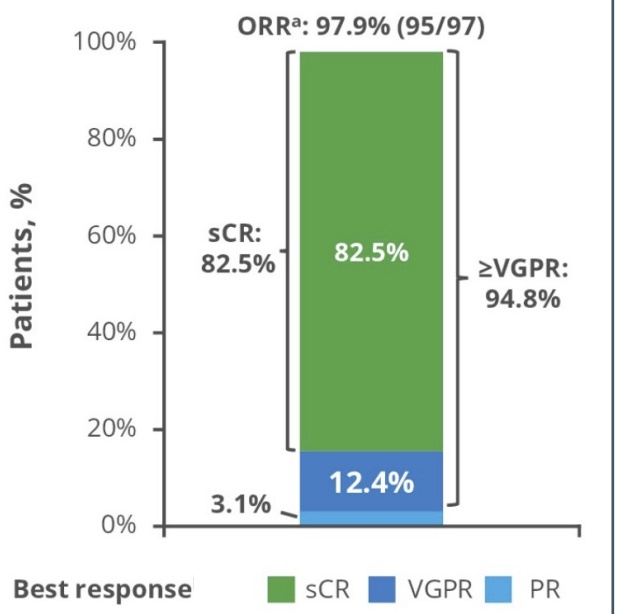
Data cutoff date: April 18, 2022.

[a] PR or better. [b] Assessed in N=225 (Ide-cel group) and N=126 (standard regimen group); 2 (1%) grade 5 CRS events occurred in the Ide-cel group. [c] 11 (4%) and 3 (2%) grade 5 infection events occurred in the Ide-cel and standard regimen group, respectively.

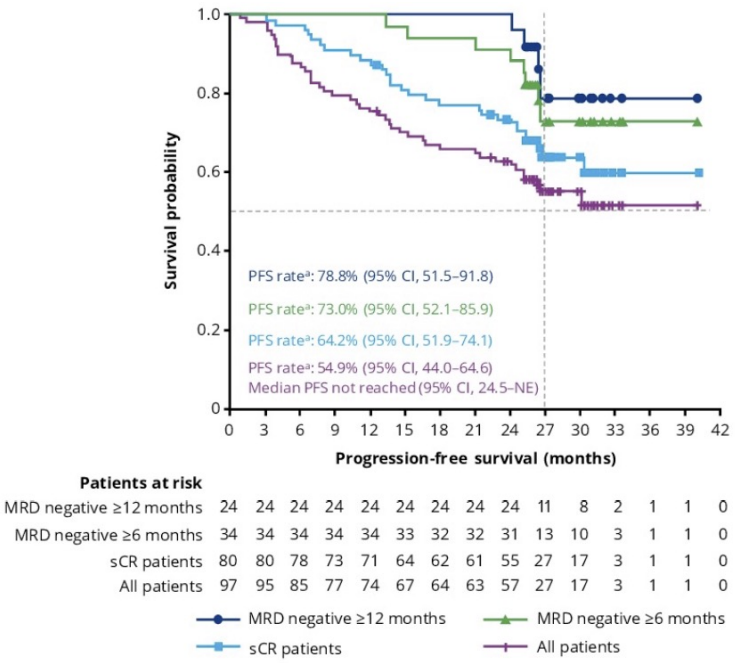
1. Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388(11):1002-1014. **2.** ClinicalTrials.gov Identifier: NCT03651128. Accessed June 15, 2023. https://clinicaltrials.gov/ct2/show/NCT03651128

Landmark 2 Years Post-Last Patient-in Results of the CARTITUDE-1 Phase 1/2 Study of Cilta-Cel in Patients With RRMM: Efficacy[1,2]

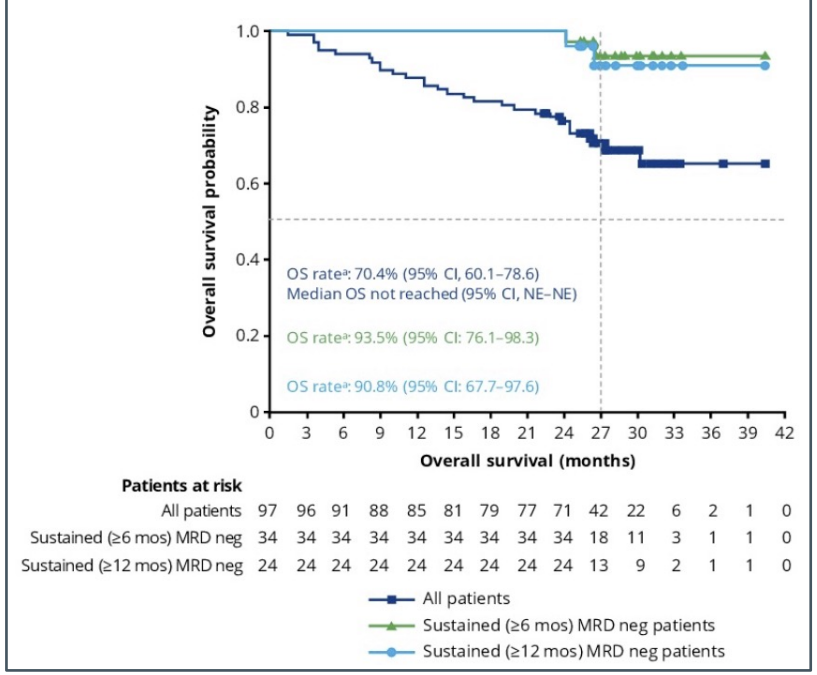
ORR BY IRC



PFS BY MRD AND RESPONSE STATUS



OS BY MRD STATUS



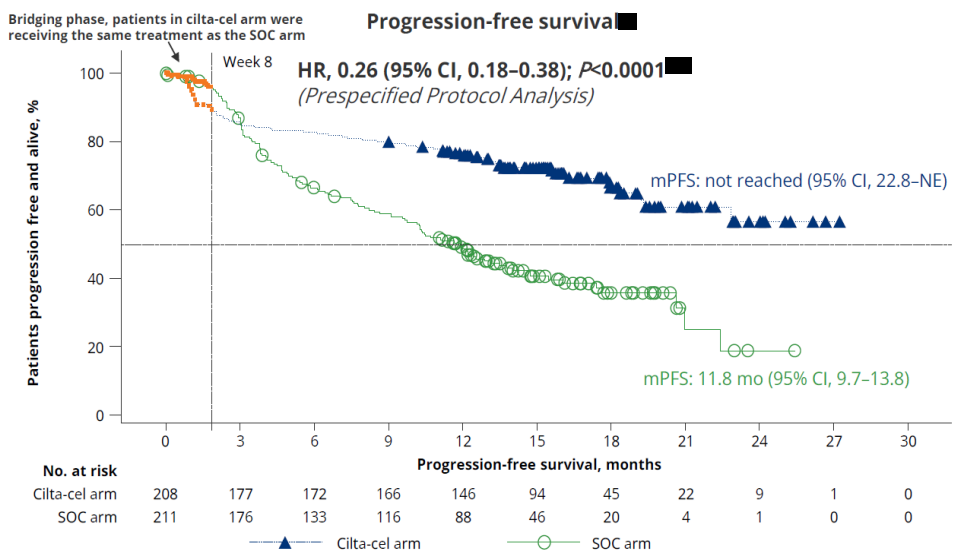
- Median DOR: NE (95% CI, 23.3 months-NE)
- Of 61 patients evaluable, 91.8% were MRD neg (10^{-5})
- DOR, PFS, and/or OS were shorter in subgroups with high-risk cytogenetics, ISS stage III, and high tumor burden, as well as presence of plasmacytomas

Data cutoff: January 11, 2022. Median follow-up: 27.7 months.
[a] 27-month PFS and OS rates.
1. Usmani SZ, et al. ASCO 2022. Abstract 8028. 2. Lin Y, et al. EHA 2022. Abstract P961.

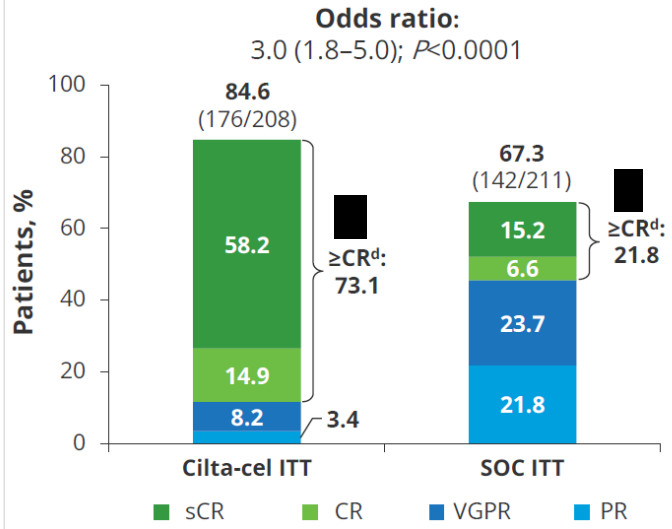
CARTITUDE-4: Cilta-Cel vs SOC in Len-Refractory RRMM

Efficacy[1,2]

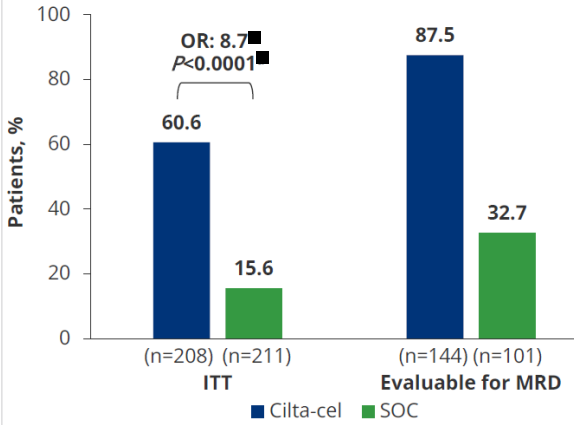
PFS



ORR



MRD Negativity at 10^{-5}



- Median follow-up: 15.9 mo (range, 0.1-27)
- 12-month PFS rate: 76% Cilta-cel vs 49% SOC
- OS data were immature
  - 39 deaths in Cilta-cel arm vs 47 deaths in SOC arm
  - HR=0.78 (95% CI, 0.5-1.2); *P*=0.26

DOR

	Cilta-Cel (n=208)	SOC (n=211)
Median DOR, mo (95% CI)	NR	16.6 (12.9-NE)
12-month DOR rate, % (95% CI)	84.7 (78.1-89.4)	63.0 (54.2-70.6)

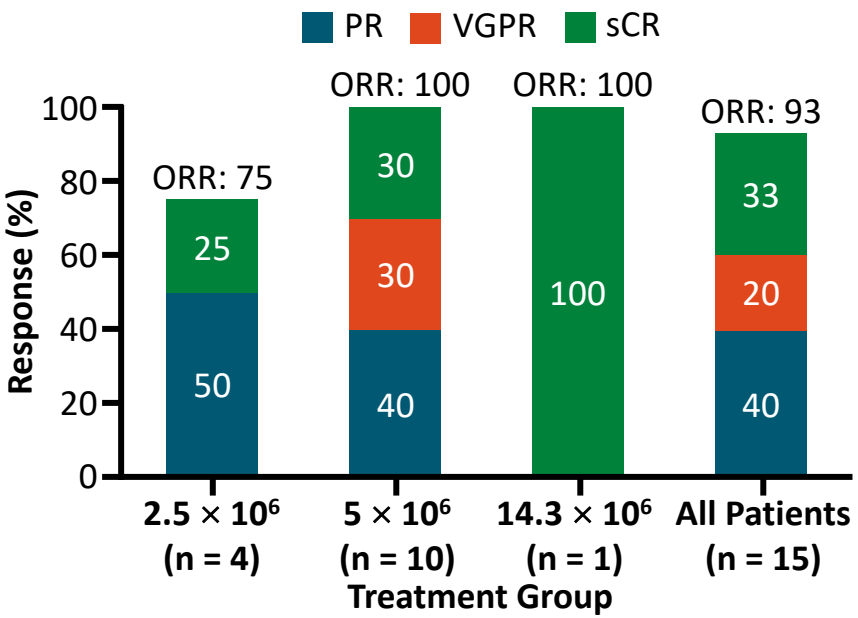
Data cutoff: November 1, 2022.

1. Dhakal B, et al. ASCO 2023. Abstract LBA106. **2.** Einsele H, et al. EHA 2023. Abstract S100.

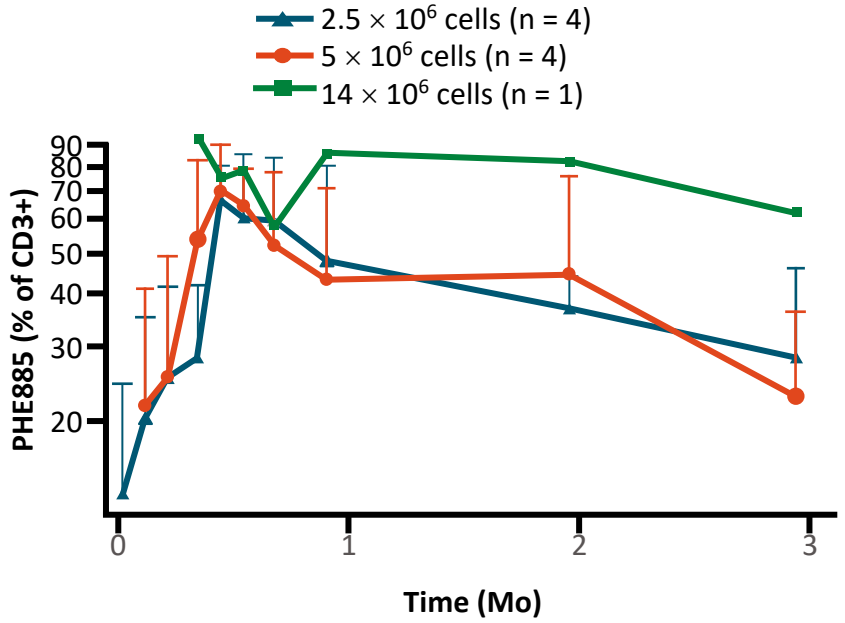
Phase I Trial of PHE885 in R/R MM: Rapid Production and Turnaround

- PHE885: anti-BCMA CAR T-cells manufactured ex vivo with culture time of approximately 24 hr; time to manufacture final product is <2 days, relying entirely on in vivo expansion after CAR T-cell infusion
- Phase I study in heavily pretreated patients with R/R MM

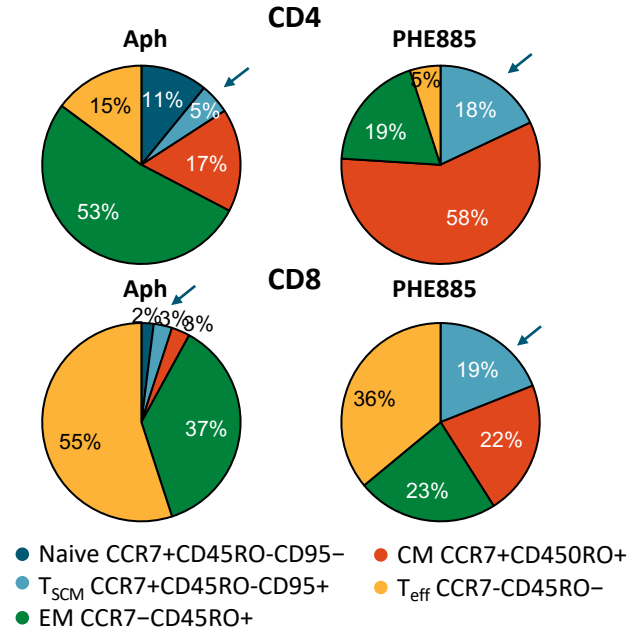
Tumor Response by Dose



Cellular Kinetics of PHE885 by Flow Cytometry



Manufacturing Process Preserves T-Cell Stemness



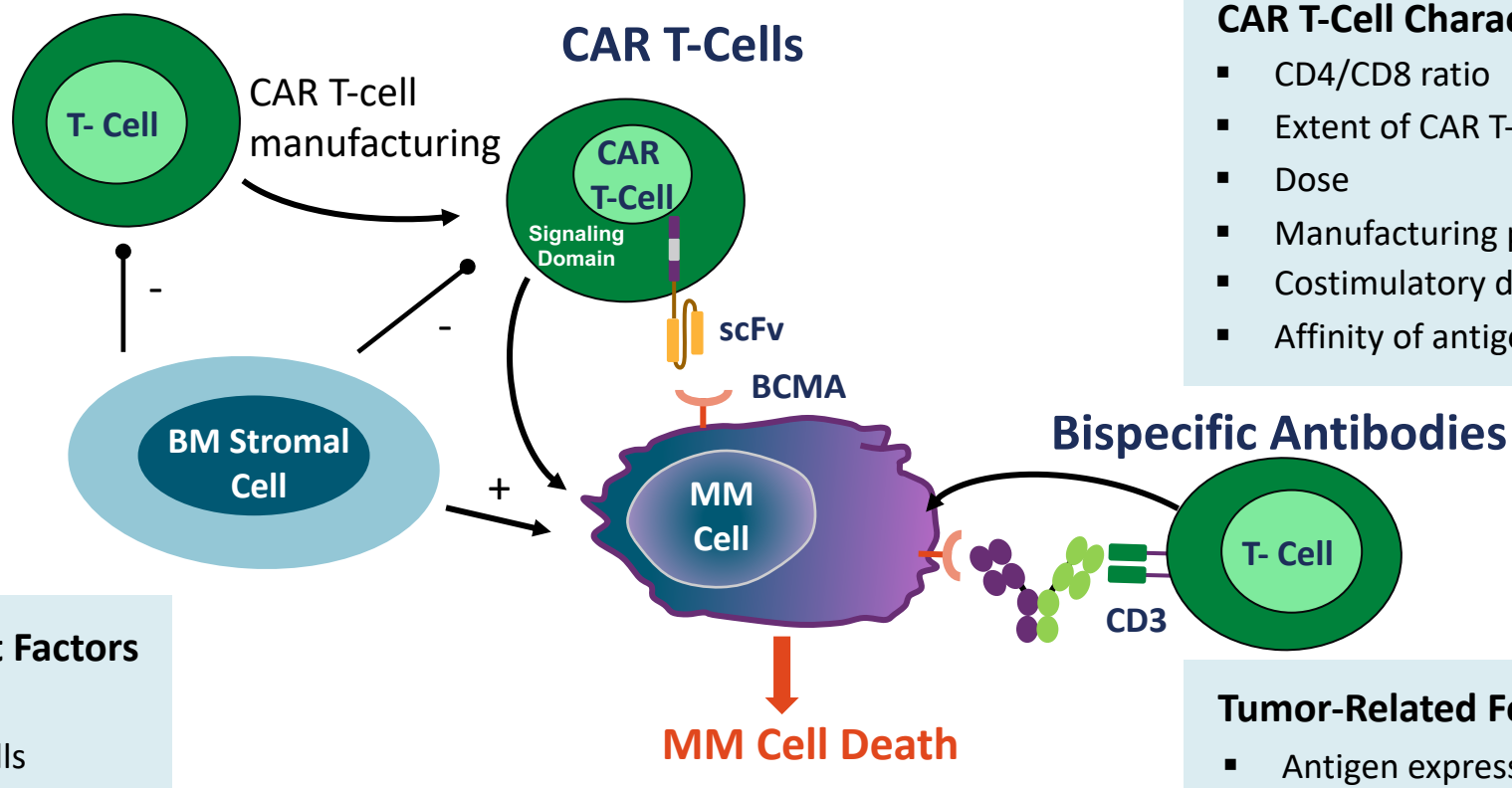
- Following PHE885 treatment, there is a shift toward naive/T_{SCM} phenotype
- Shift to T_{SCM}/T_{naive} population observed in CD4+ and CD8+ T-cells in patients with ≥ VGPR but not wi

Sperling. ASH 2021. Abstr 3864.

BCMA Immunotherapy Treatment Failure

Premanufacturing T-Cell Characteristics

- Absolute T-cell count
- CD4/CD8 ratio
- Impact of prior therapy on T-cell fitness
- Proportion with early memory phenotype



CAR T-Cell Characteristics

- CD4/CD8 ratio
- Extent of CAR T-cell exhaustion
- Dose
- Manufacturing process
- Costimulatory domain
- Affinity of antigen-binding domain

MM Microenvironment Factors

- BM stromal cells
- Immune suppressor cells
- Bridging therapy
- Lymphodepleting conditioning regimen

Tumor-Related Features

- Antigen expression levels
- Tumor load
- High-risk cytogenetics
- Extramedullary disease

Niels. Blood Cancer Discov. 2021;2:302.

Slide credit: clinicaloptions.com

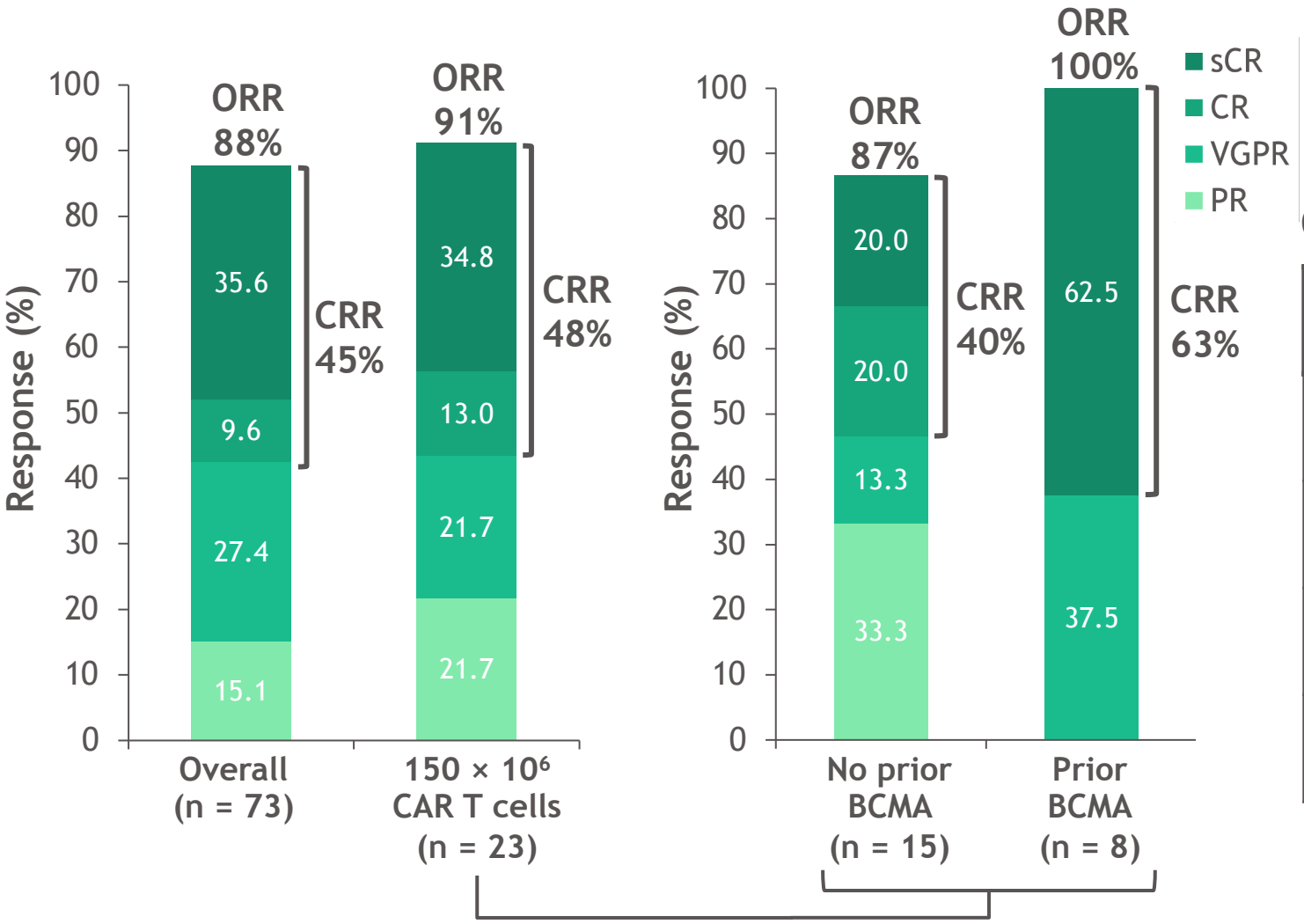
BMS-986393 (CC-95266), a G protein–coupled receptor class C group 5 member D–targeted chimeric antigen receptor T-cell therapy for relapsed/refractory multiple myeloma: updated results from a phase 1 study

Susan Bal,[1] Myo Htut,[2] Omar Nadeem,[3] Larry D. Anderson, Jr,[4] M. Hakan Koçoğlu,[5] Tara Gregory,[6] Adriana C. Rossi,[7] Tom Martin,[8] Daniel N. Egan,[9] Luciano J. Costa,[1] Hongxiang Hu,[10] Yanping Chen,[10] Shaoyi Li,[10] Lisa M. Kelly,[10] Naomey Sarkis,[10] Safiyyah Ziyad,[10] Wei-Ming Kao,[10] Allison J. Kaeding,[10] Michael R. Burgess,[10] Jesus G. Berdeja[11]

[1]University of Alabama at Birmingham, Birmingham, AL, USA; [2]City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [3]Dana–Farber Cancer Institute, Boston, MA, USA; [4]Hematologic Malignancies and Cellular Therapy Program, Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX, USA; [5]University of Maryland, Baltimore, MD, USA; [6]Colorado Blood Cancer Institute, Sarah Cannon Cancer Network, Denver, CO, USA; [7]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [8]University of California, San Francisco, CA, USA; [9]Swedish Cancer Institute, Seattle, WA, USA; [10]Bristol Myers Squibb, Princeton, NJ, USA; [11]Tennessee Oncology and Sarah Cannon Research Institute, Nashville, TN, USA

ASH 2023, Presentation number 219

BMS-986393 in RRMM: high response rates irrespective of prior BCMA-targeted therapy or high-risk features[a]



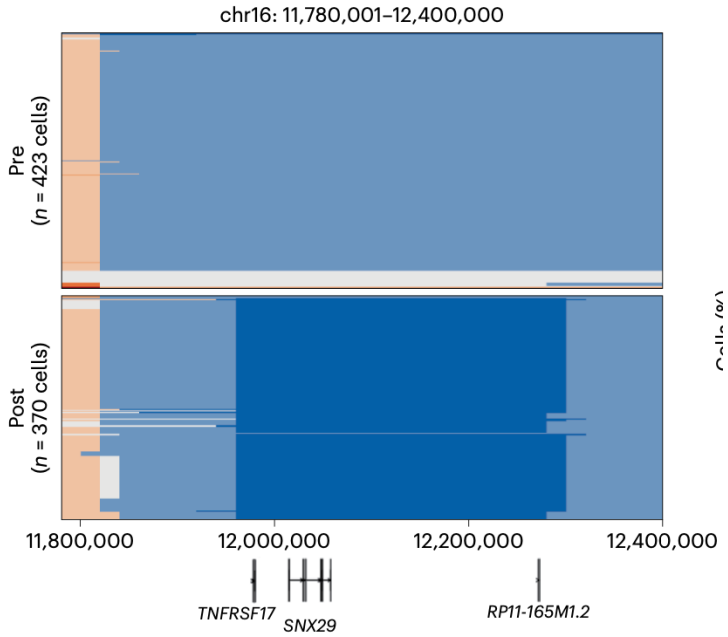
ORR in subgroups of interest (all dose levels)

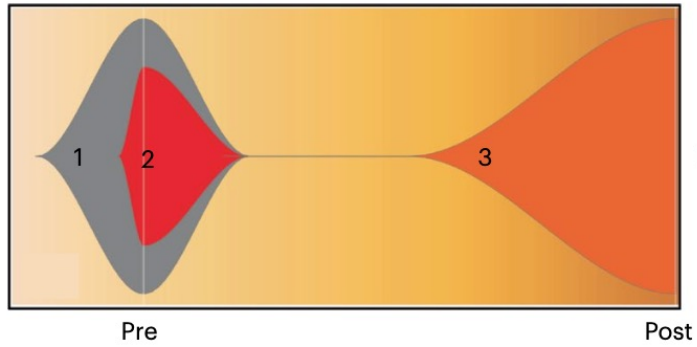
Disease characteristic, % (n/N)	Present	Absent
Prior BCMA treatment	78% 25/32	95% 39/41
Extramedullary disease	84% 26/31	91% 38/42
High-risk cytogenetics[b]	83% 24/29	91% 40/44
Triple-class refractory	88% 50/57	88% 14/16

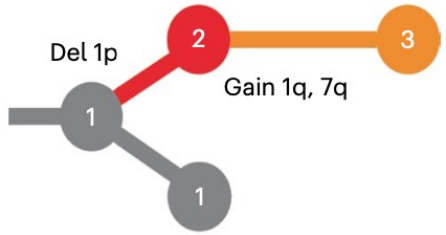
Data cutoff: September 11, 2023. [a]The efficacy-evaluable analysis set includes all patients who received conforming BMS-986393 cell product, had measurable disease at the last disease assessment prior to BMS-986393 infusion, and had ≥ 1 post-infusion disease response assessment. Responses were assessed per International Myeloma Working Group criteria.
[b]del(17p), t(4;14), and/or t(14;16).
CR, complete response; CRR, complete response rate; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

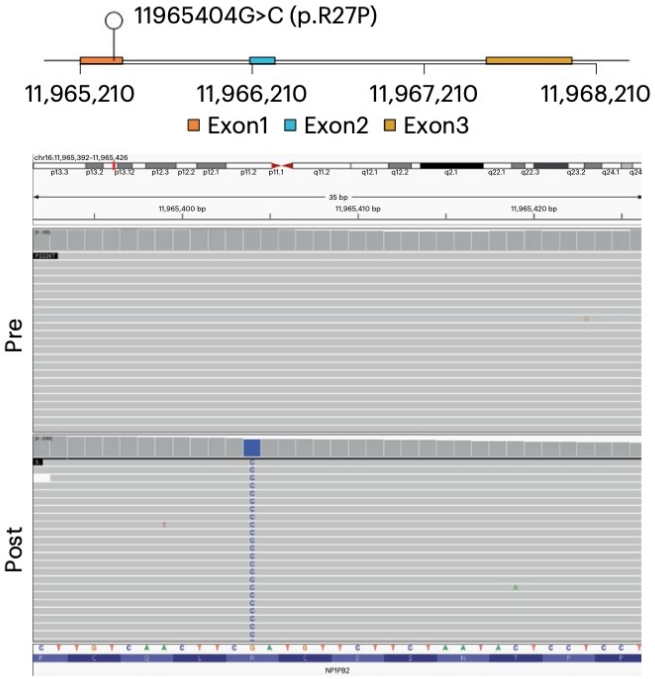
Bal S, et al. ASH 2023 [Presentation 219]

GENOMIC CHANGES CAN DRIVE RESISTANCE









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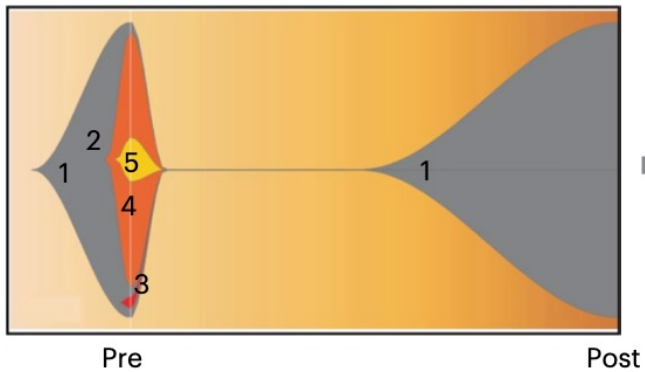
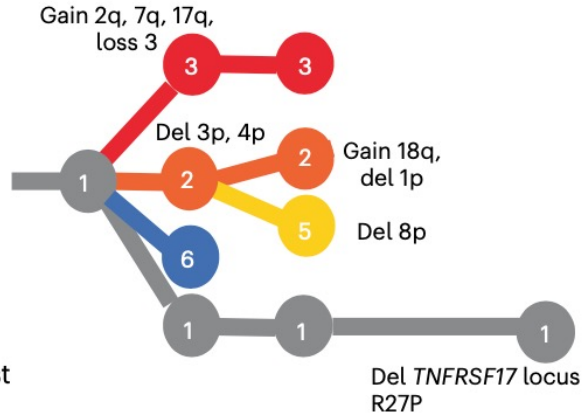
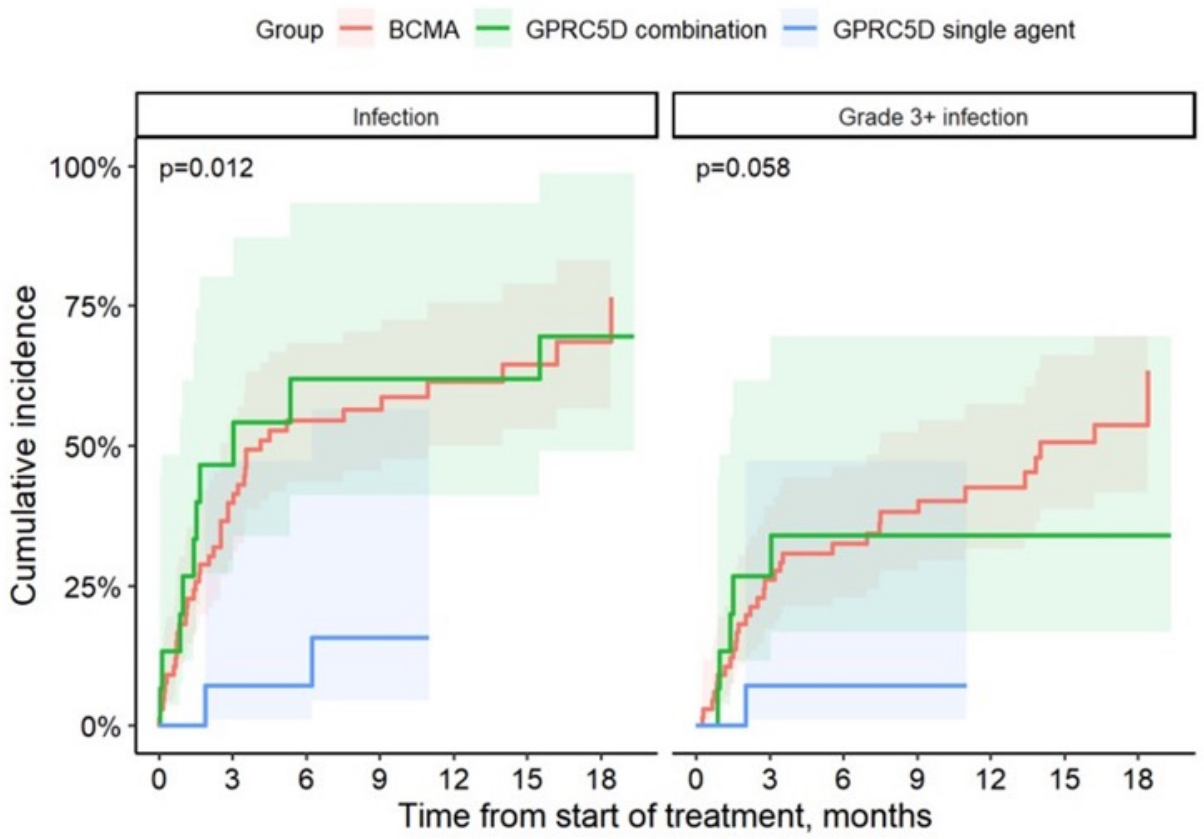
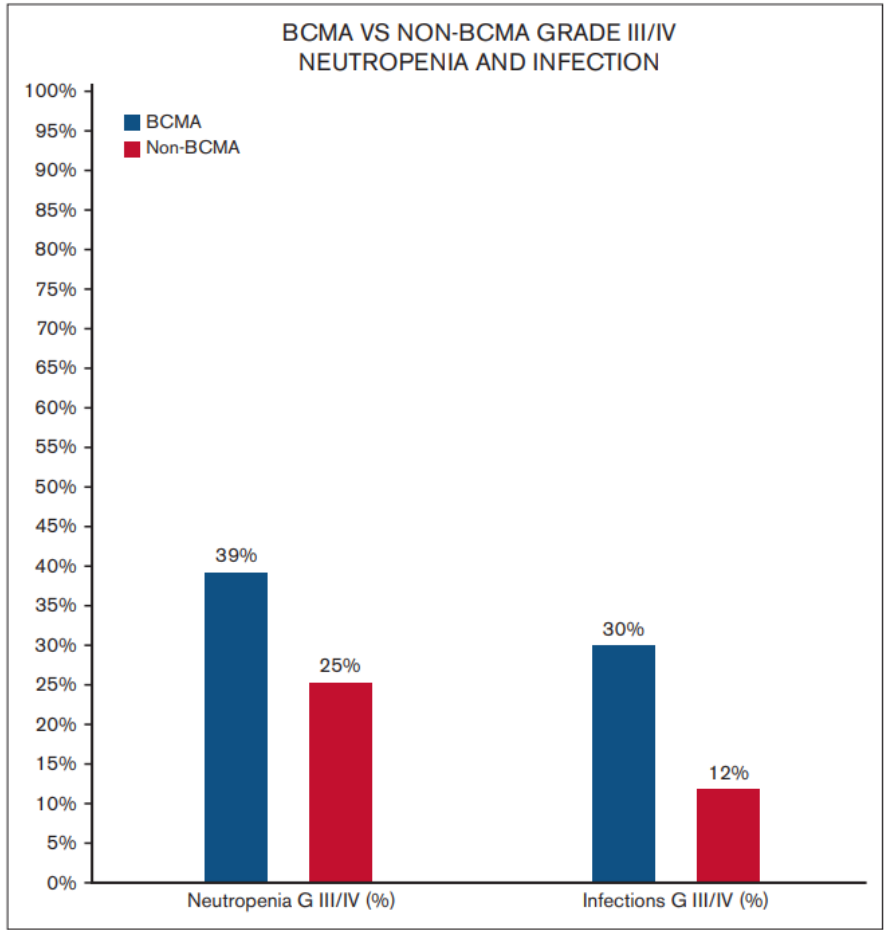




LEE ET AL, *NATURE MEDICINE* 2023

Risk of infection varies depending on the type of bsAb therapy used





- **BCMA vs. GPRC5D: higher infections with BCMA**
- Grade 5 events were observed in 8% of patients with BCMA bispecific antibodies and none with GPRC5D bispecific antibodies

Mazahreh et.al. Blood Advances 2023; Janardan et al., ASC0 2023

Neutralizing antibodies to COVID are blocked by potent Immune therapies

Treatment			
Line 1—including maintenance	100	2.00 (1.05 to 3.79)	.034
Line 2+ with anti-CD38 mAb	72	0.53 (0.27 to 1.05)	.069
Line 2+ without anti-CD38 mAb	66	—	—

Nooka et al, JCO 2021

Immune therapy circa 2021

- We now have multiple immune targets including CD38, SLAMF7, BCMA, GPRC5d and FCRH5
- Their expression is somewhat consistent across different genetic and treatment groups.
- Focus now needs to be on a strategy for integration of target and modality (CART vs Bispecific vs MOAB) and how we can enhance immune function to best optimize each of the above approaches.

What does the future hold?

- Change the paradigm in several ways
  - Challenge ourselves to test limited duration therapy as the model
  - Consider paired or sequential immune targets with agents primed to enhance immune function/reduce exhaustion
  - Understand how best to use precision medicine when clonal burden is lower

Patients and Families

Thanks to:

Jonathan Kaufman
Ajay Nooka
Craig Hofmeister
Madhav Dhodapkar
L.T. Heffner
Vikas Gupta
Nisha Joseph
Leon Bernal
Charise Gleason
Danielle Roberts
Donald Harvey
Amelia Langston
Y. Gu
S-Y Sun
Jing Chen
Mala Shanmugan
Larry Boise
Bryan Burton
Sam Gagnon

IMS

Golfers Against Cancer
T.J. Martell Foundation

And Many Others who
are part of the Myeloma clinical and
research tam

sloni01@emory.edu