How to Integrate Novel Approaches in the Treatment of Relapsed/Refractory Multiple Myeloma

Kenneth Anderson, MD
Director, Jerome Lipper Multiple Myeloma Center
and LeBow Institute for Myeloma Therapeutics
Dana-Farber Cancer Institute
Kraft Family Professor of Medicine
Harvard Medical School

Disclosures

Consultant: Pfizer, Amgen, Astrazeneca, Janssen, Precision Biosciences, Mana, Window, Starton

Speaker's Bureau: none

Grant/Research Support: none

Founder/ Stock Shareholder: C4 Therapeutics, Oncopep, Raqia, NextRNA

Honoraria: As per consultants above

Full-time/Part-Time Employee: none

Other: none

Therapy for Newly Diagnosed MM Transplant Candidates

Triplets

Lenalidomide (R)/ Bortezomib (V)/ Dexamethasone (Dex) RVD
Cyclophosphamide (Cy)/Bortezomib/Dex CyBorD
Carfilzomib (K) RD if neuropathy KRD
Ixazomib RD all oral IRD
VRD equivalent to KRD in non high risk; KRD in high risk

Quadruplets

VTD-Daratumumab (Cassiopeia, MRD- responses, FDA approved)
RVD-Dara (Griffin, MRD- responses)
KRD-Dara (Forte, MRD- including high risk)
Elotuzumab RVD equivalent to RVD in high risk
Isatuximab KRD active in high risk
Ixazomib RD Dara under evaluation

Maintenance

R in standard risk; VR Bort, KR, Dara-R in high risk

Therapy for Newly Diagnosed MM Transplant Ineligible

Triplets preferred at attenuated dose/schedule:

Lenalidomide (Len)/ Bortezomib (Bort)/ Dexamethasone (Dex) RVD Lite

Cyclophosphamide (Cy)/Bort/Dex CyBorD

Carfilzomib RD if neuropathy KRD

Ixazomib RD all oral regimen IRD

Daratumumab RD DRD (Maia, FDA approved)

Doublets

Frail patients, ie Bort/Dex or Len/Dex at reduced doses

Quadruplet

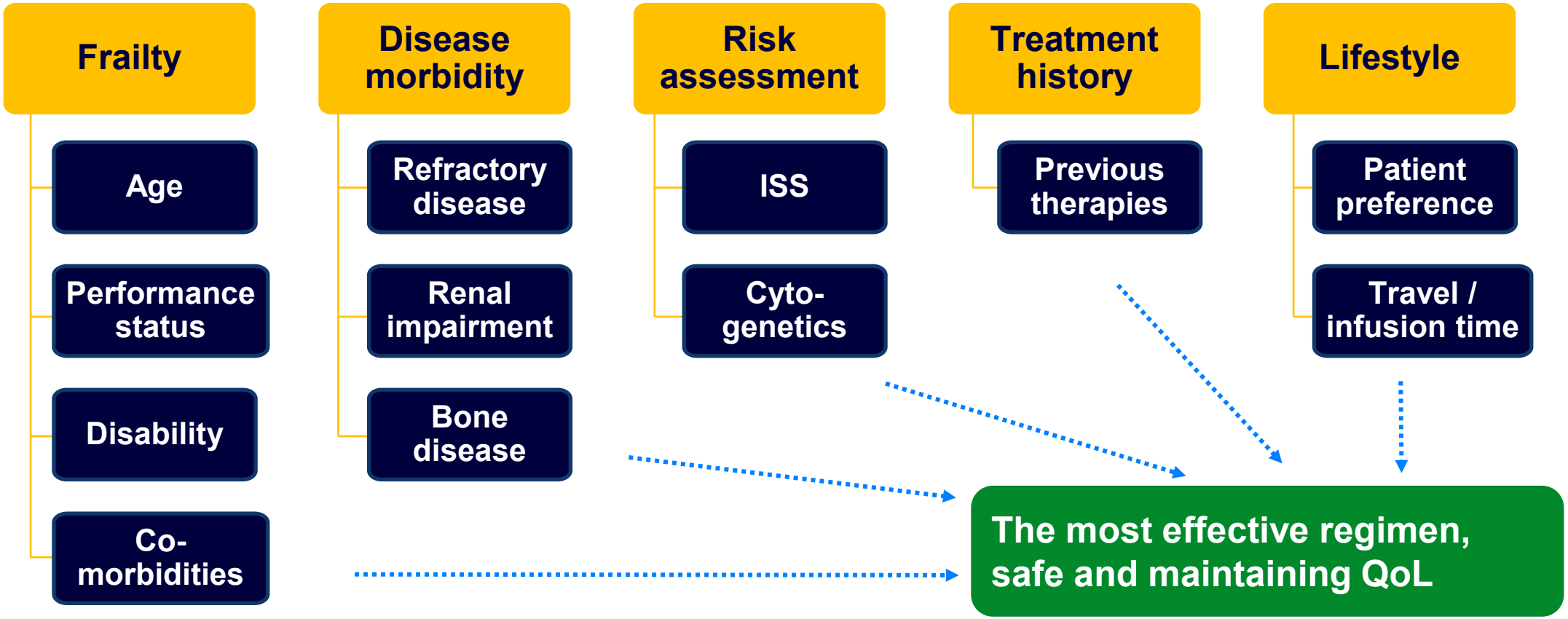
Daratumumab MPV (FDA approved but not used in USA); RVD lite,

R ixazomib D with or without MoAbs under evaluation

Maintenance

Len in standard risk, Bort or Len Bort in high risk, MoAbs under evaluation

Disease and Patient Factors Influence Treatment Choices in Relapsed Refractory MM



Therapy for Relapsed MM:Triplets Preferred With Second Generation IMiDs, PIs, MoAbs

Active In Len and Bort refractory MM

Carfilzomib Pom Dex (no neuropathy)

Dara Pom Dex (FDA approved), Dara Carfilzomib Dex (deep responses, FDA approved)

Elo Pom Dex (well tolerated, FDA approved)

Isatuximab Pom Dex (FDA approved) Isa Carfilzomib Dex (FDA Approved)

Active in Bort refractory MM

Elotuzumab Len/Dex (indolent relapse), Ixazomib Len Dex (all oral), Carfilzomib Len Dex (no neuropathy), Dara Len dex (MRD- responses) (all FDA approved)

Active in Len refractory MM

Pom Bort Dex, Dara Bort Dex (MRD- responses)(FDA approved)

Active in Len, Pom, Bort, Carfil, Dara refractory MM

Selinexor (GI side effects), Belantomab mafodotin (keratopathy), Idecel CAR T cells (all FDA approved)

Randomized Studies With Bortezomib-Dexamethasone Control Arms (Includes lenalidomide refractory MM)

	Pomalidomide		Daratumumab*		Carfilzomib		Selinexor		Venetoclax	
N	PVd vs Vd 559		DVd vs Vd 498		Kd vs Vd 929		SVD vs Vd 195 vs 207		VenVD vs VD 194 vs 97	
Efficacy	**Tx**	**Control**	**Tx**	**Control**	**Tx**	**Control**	**Tx**	**Control**	**Tx**	**Control**
Median follow up, mos	16		26.9		37.5		16.5		18.7	
ORR	82%	50%	85%	63%	76%	63%	76%	62%	82%	68%
CR	16%	4%	30%	10%	13%	6%	17%	11%	13%	1%
Median PFS, mos	11	7	16.7	7.1	18.7	9.4	13.93	9.46	22.4	11.5
PFS HR (95% CI)	0.61 (0.49–0.77)		0.32 (0.25–0.40)		0.53 (0.44–0.65)		0.70		0.63	
Median OS, mos	NR	NR	NR	NR	47.6	40.0	NR	25	NR	25
OS HR (95% CI)	NR		NR		0.79 (0.65-0.96)				**2.03 (1.04-3.95)**	

*Vd 8 *21 day cycles

t(11;14):
PFS HR 0.11
OS HR 0.343

Daratumamab refractory patients excluded in CASTOR trial, not represented in others

Richardson et al. Lancet Oncol 2019; 20: 781–94; Palumbo A et al. *N Engl J Med*. 2016;375:754; Spencer A et al. *Haematologica*. 2018; Sep 20 [epub ahead of print]; Dimopoulos MA et al. *Lancet Oncol*. 2016;17:27; Dimopoulos et al ASCO 2020; Kumar, S EHA 2019

Randomized Studies With Lenalidomide-Dexamethasone Control Arms (FDA approved, includes Bort refractory MM)

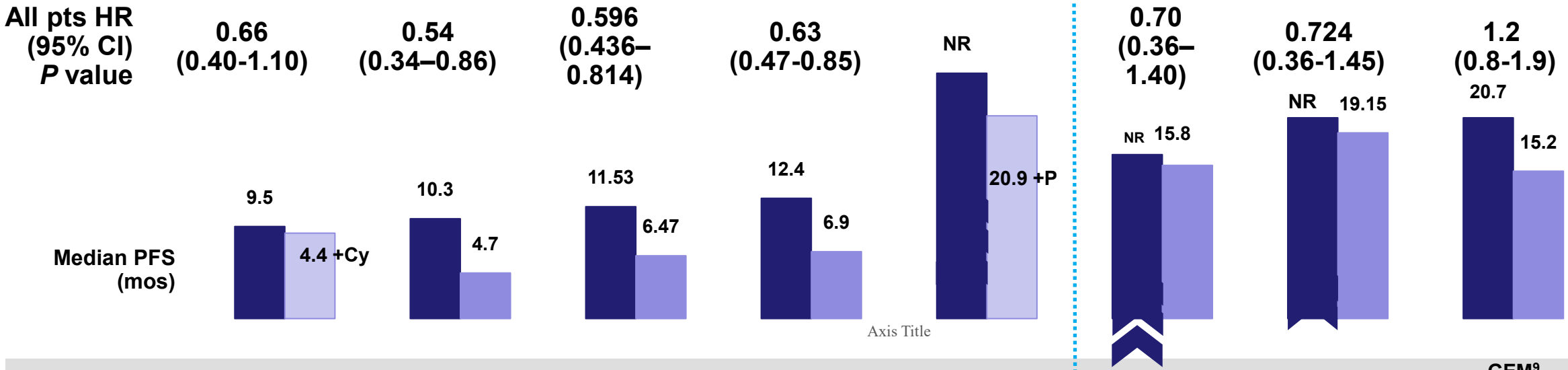
	Ixazomib		Elotuzumab		Carfilzomib*		Daratumumab	
N	IRd vs Rd 722		ERd vs Rd 646		KRd vs Rd 792		DRd vs Rd 569	
Efficacy	Tx	Control	Tx	Control	Tx	Control	Tx	Control
Median follow up, mos	23		Min 48 mos		67		32.9	
ORR	78.3%	71.5%	79%	66%	87.1%	66.7%	93%	76%
CR	12%	7%	5%	9%	32%	9.3%	55%	23%
Median PFS, mos	21	14.7	19	14.9	26	16.6	NR	17.5
PFS HR (95% CI)	0.74 (0.59–0.94)		0.71 (0.59–0.86)		0.69 (0.57–0.83)		0.44 (0.34–0.55)	
Median OS, mos	NR	NR	48.3	39.6	48.3	40.4	NR	NR
OS HR (95% CI)	NR		0.78 (0.63–0.96)		0.79 (0.67-0.95)		NR	

*PFS HR 0.5 @ 18 mos8

NB Daratumumab refractory patients not included in POLLUX or ELOQUENT trials

Moreau P et al. *N Engl J Med*. 2016;374:1621; Dimopoulos MA et al. *Br J Haematol*. 2017;178:896; Stewart AK et al. *N Engl J Med*. 2015;372:142; Stewart AK et al. *Blood*. 2017;130: Abstract 743.; Dimopoulos M et al. *J Hematol Oncol*. 2018;11:49; Dimopoulos MA et al. N Engl J Med. 2016;375:1319.

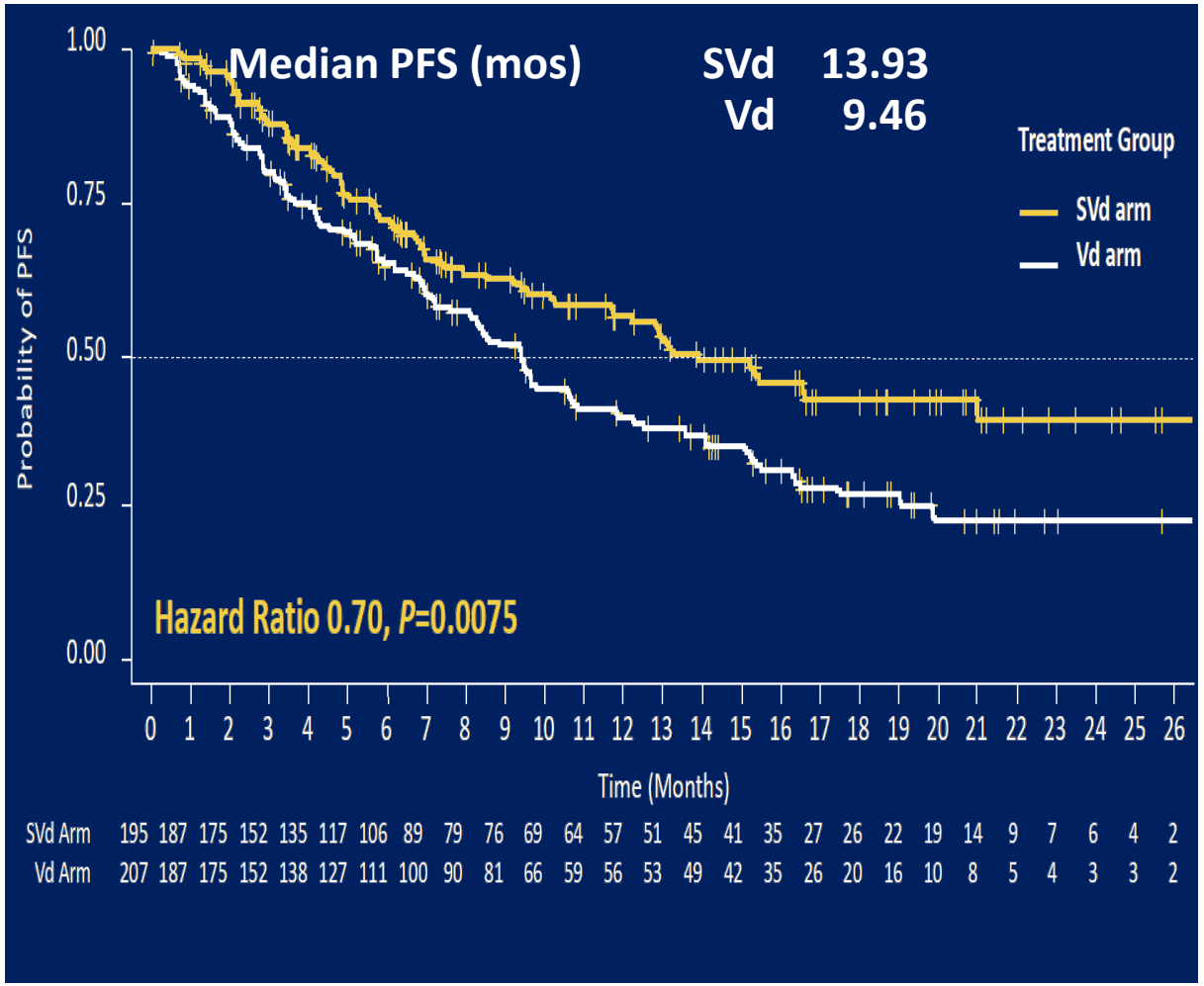
Pomalidomide/Carfilzomib Backbone Randomized Studies

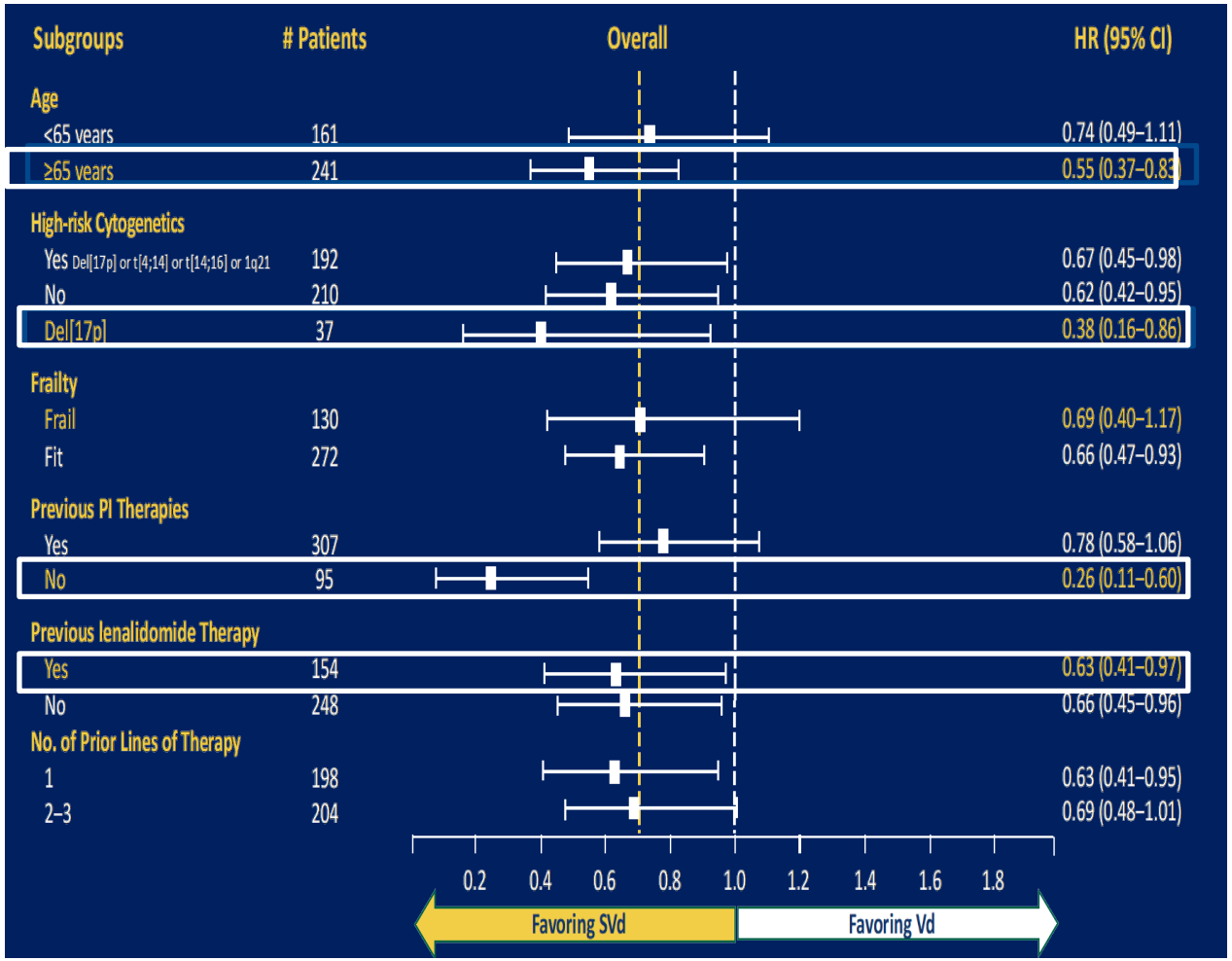


	PomCyDex vs PomDex+Cy[1]	ELOQUENT-3[2] EPd vs Pd	ICARIA-MM[4] Isa-Pd vs Pd	APOLLO[5] D-Pd vs Pd	DCdP vs DCd+P[6]	CANDOR[7] DKd vs Kd	IKEMA[8] IsaKd vs Kd	GEM[9] KyCydex vs Kydex
Total N	34 vs 36	60 vs 57	154 vs 153	151 vs 153	61 vs 59	312 vs 154	179 vs 123	97 vs 101
No. prior lines	4	3	3	2	2	2	2	1
Len refractory (%)	100	90 vs 84	94 vs 92	79.6	97	32 vs 36	31.8 vs 34.1	33 vs 36
PI refractory (%)	78 vs 71	78 vs 82	77 vs 75	48	93			92
mFU (months)		9.1	11.6	16.9	25.3 (8.9 mo after +P in Arm B)	16.9 vs 16.3	20.7	15.6
≥CR (%)	3 vs 3	8 vs 2	5 vs 1	24.5 vs 3.9		29 vs 10	39.7 vs 27.6	18 vs 20
OS HR	0.63 (0.32-1.22)	NR	NR	0.91 (0.61-1.35)	NR			P=0.9
Missing Molecular Data (%)			18 vs 26			51 vs 49	12.8 vs 11.4	24.7 vs 21.7

1. Baz RC et al. Blood (2016) 127 (21): 2561–2568; 2. Dimopoulos MA et al. N Engl J Med. 2018;379:1811; 3. Richardson et al. Lancet Oncol. 2019;20:781-794; 4. Attal M et al. *Lancet*. 2019;394:2096;
5. Dimopoulos MA et al. ASH 2020; 6. Sebag M et al. ASH 2020. 7. Dimopoulos M et al. Lancet. 2020;396:186; 8. Moreau P et al. Presented at the 25th European Hematology Association Annual Meeting; June 2020. Abstract LB2603.
9. Mateos MV et al. ASH 2020.

BOSTON Trial: Selinexor-Vd vs Vd in Patients with Multiple Myeloma Who Had Received 1-3 Prior Therapies (FDA Approved)



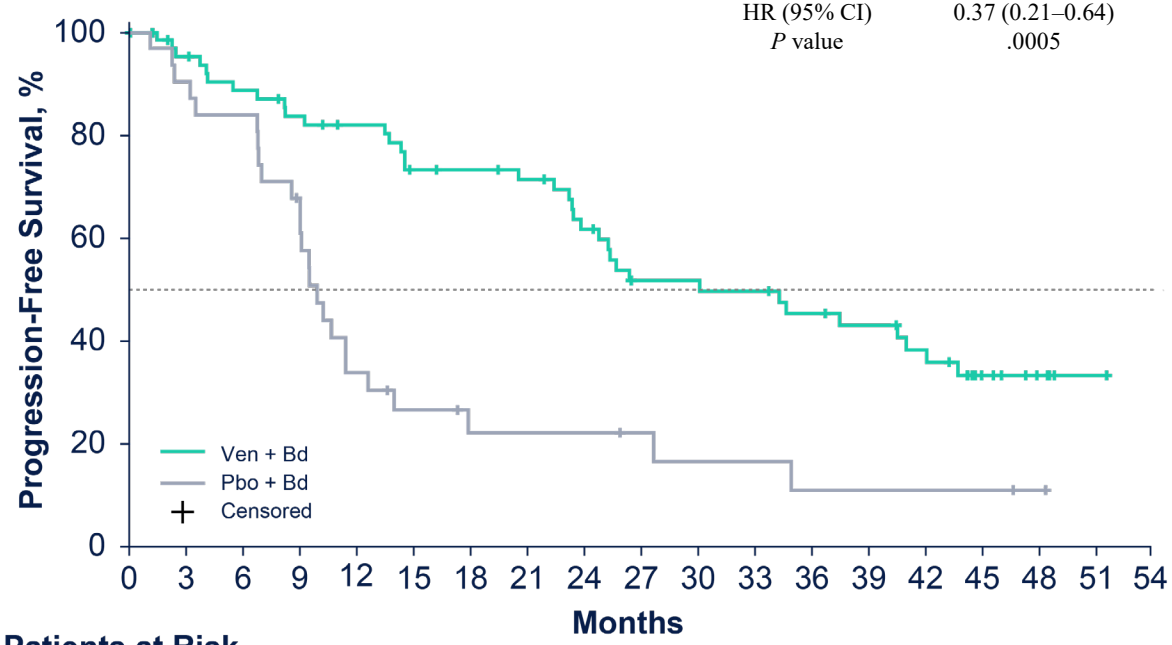


Dimopoulos MA et al Lancet 2020; 396: 1563-73.

Among patients with *BCL2*^{high} expression, median PFS was 30.1 months in the Ven + Bd arm compared with 9.9 months in the Pbo + Bd arm (*P*=.0005)

Investigator-Assessed PFS in Patients With *BCL2*^{high}

PFS	Ven + Bd	Pbo + Bd
Median, months	30.1	9.9
HR (95% CI)	0.37 (0.21–0.64)	
P value	.0005	

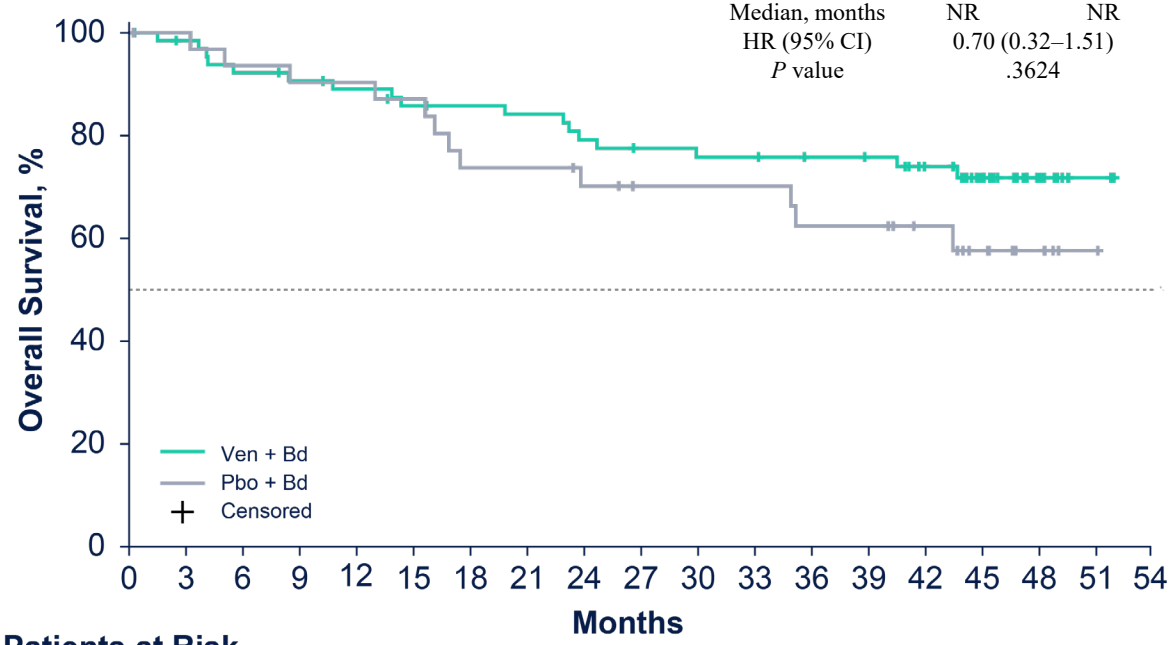


Patients at Risk

66	59	54	50	47	41	40	38	32	25	25	24	21	19	16	9	4	1	0
32	28	26	20	10	7	5	5	5	4	3	3	2	2	2	2	1	0	

OS in Patients With *BCL2*^{high}

OS	Ven + Bd	Pbo + Bd
Events	17	12
Median, months	NR	NR
HR (95% CI)	0.70 (0.32–1.51)	
P value	.3624	



Patients at Risk

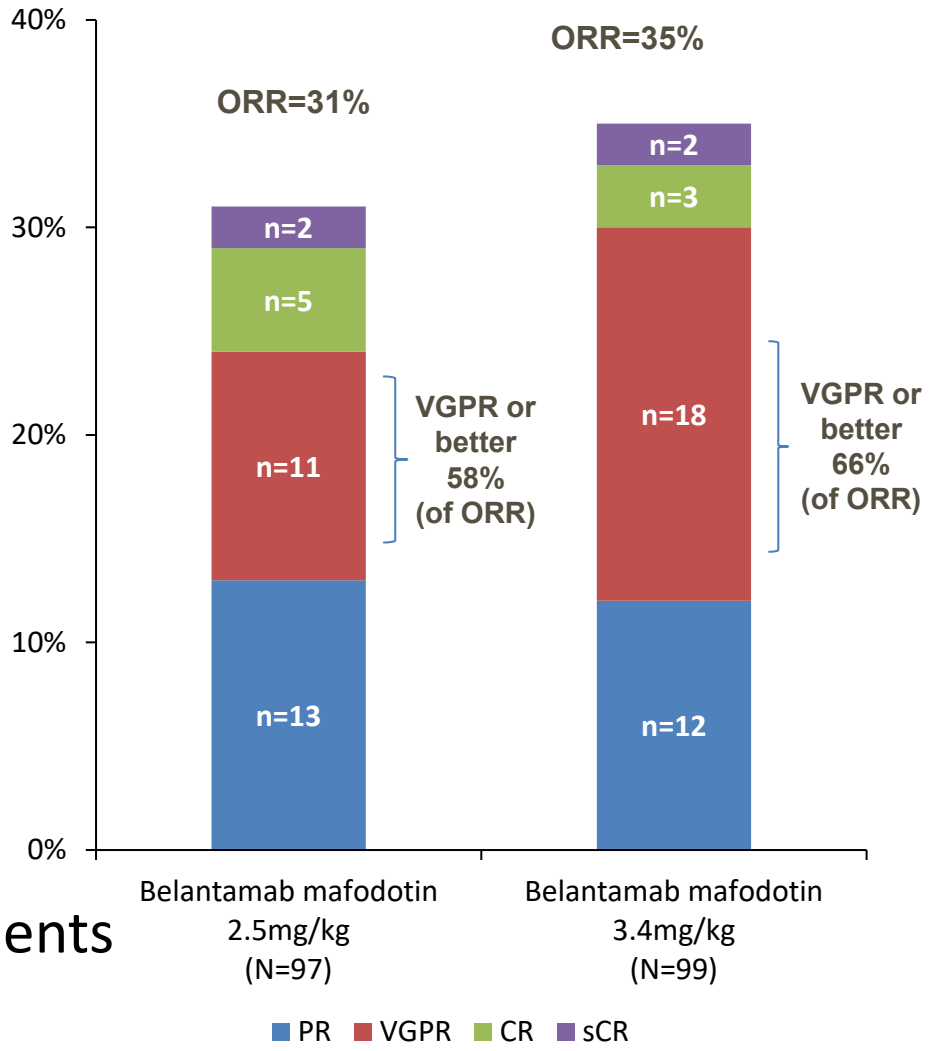
66	63	59	57	55	53	52	51	48	45	44	44	42	41	37	26	11	2	0
32	31	29	28	28	26	22	22	20	18	18	18	16	16	13	9	5	1	0

Bd, bortezomib + dexamethasone; HR, hazard ratio; NR, not reached; OS, overall survival; Pbo, placebo; PFS, progression-free survival; Ven, venetoclax.

Kumar et al, ASH 2021

BCMA Immuntoxin: Belantamab Mafodotin 3.4mg/kg vs 2.5-mg/kg in RRMM (13 month followup) (FDA Approved 2020)

	belantamab mafodotin 2.5mg/kg (n=97)	belantamab mafodotin 3.4mg/kg (n=99)
mOS	14.9 months (95% CI: 9.9-NR)	14.0 months (95% CI: 10-NR)
mDOR	**11.0 months (95% CI: 4.2-NR)**	6.2 months (95% CI: 4.8-NR)
mPFS	2.8 months (95% CI: 1.6-3.6)	3.9 months (95% CI: 2.0-5.8)
ORR*	31% (97.5% CI: 21.7-43.6)	35% (97.5% CI: 24.8-47.0)



Keratopathy 27% (2.5mg/kg) and 21% (3.4mg/kg) patients

2.5mg/kg chosen for further studies

Lonial et al Lancet Oncol 2020; 21: 207-21.; ASCO 2020

CAR T-Cell Therapy in Multiple Myeloma

FDA Approved

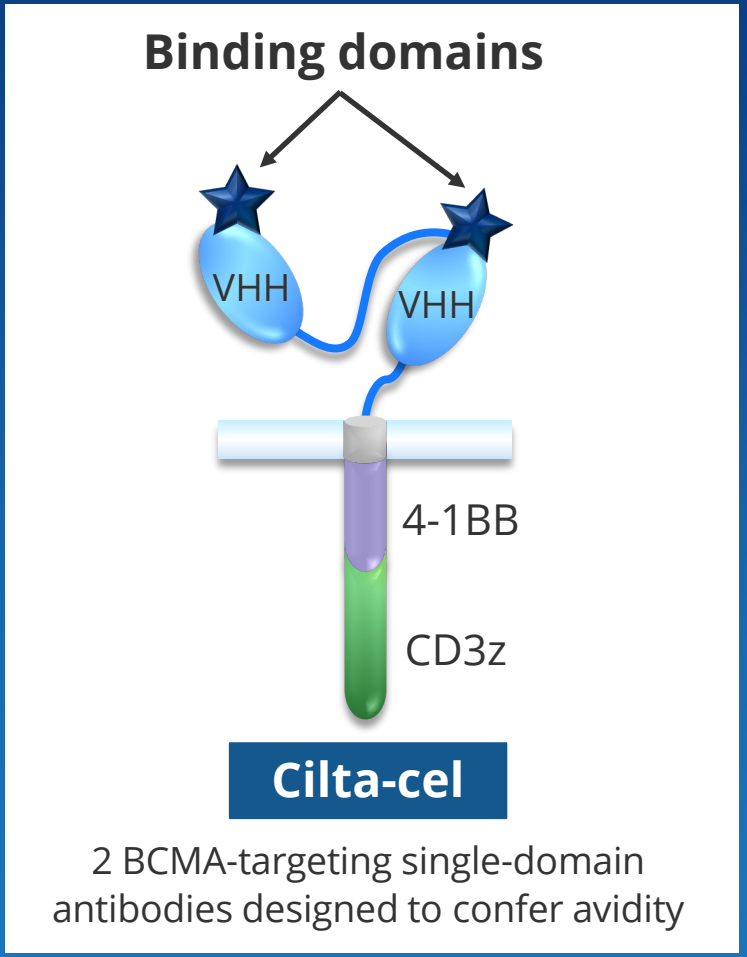
	Ide-cel Ph1 N=128	Cilta-cel Ph1b/2 N=97	Orva-cel Ph1b/2 N=62	bb21217 Ph1 N=72	CT053 Ph1b/2 N=20	P-BCMA-101 Ph1/2 N=55	GC012F Ph1 N=16	GPRC5D Ph1 N=18	ALLO-715 Ph1 N=31
CRS, % **All grades** **Grade ≥3**	84% 5%	9% 4%	89% 3%	70% 4%	77% / 83%[a] 0% / 0%	17% 0%	100% 13%	92% 5%	52% 3%
NT, % **All grade** **Grade ≥3**	18% 3%	21% 0.5%	13% 3%	16% 4%	15% / 17%[a] 8% / 0%	4% 4%	0 0	0 0	3% 0
ORR **CR**	73% ≥CR 33% (450: OR 81%, CR 39%)	97.9% ≥sCR 82.5%	92% CR 36%)	75% (≥CR 28%)	94% (≥CR 28%)	44% - 75%[b]	94% (≥CR 56%)	83%	61% in DL3 or DL 4 (n=26)
Median follow-up	13.3 mo	24.0 mo		5.8 mo	6 mo	120-508 days[b]	7.3 mo	13 wks	7.4 mo
Median DOR	10.7 mo (450: 11.3 mo)	21.8-NE mo	Not reported	17.0 mo	Not reported	Not reported	Not reached	Not reached	8.3 mo
Median PFS	8.6 mo 12.2 mo 20.2 CR/sCR	All : NR sCR: NR, 70% at 2 yrs	Not reported	Not reported	Not reported	Not reported	Not reported		Not reported
Median OS	24.8 mo	74% at 2 yrs Median NR	Not reported	Not reported	Not reported	Not reported	Not reported		Not reported

Munshi et al NEJM 2021; 705-16; Berjeda et al Lancet 2021; 398:314-24.; Lin et al; Alsina et al; Kumar et al; Costello et al; Jiang et al; Mailankody et al; Anderson et al; Usmani et al ASH/ASCO 2020,2021; Martin et al; Raje et al; Mailankody et al, ASH 2021

CARTITUDE-1: Introduction

Ciltacabtagene autoleucel (cilta-cel; JNJ-68284528) is a chimeric antigen receptor T-cell therapy for the treatment of patients with RRMM[1]

- In the phase 1b/2 CARTITUDE-1 study, early, deep, and durable responses were observed with a single cilta-cel infusion in heavily pretreated patients with RRMM[1]
  - At a median follow-up of 12.4 months
    - Cilta-cel had a manageable safety profile
    - ORR and sCR were 97% and 67%, respectively
    - Overall 12-month PFS and OS rates were 77% and 89%, respectively
    - Median PFS and duration of response were not reached (95% CI, 16.8–not estimable and 15.9–not estimable, respectively)
- **Here, we report updated results from the CARTITUDE-1 study with a longer duration of follow-up (median ~2 years)[a]**



Martin et al ASH 2021

CARTITUDE-1: Conclusions

At a median follow-up of ~2 years patients treated with cilta-cel showed durable and deepening responses

- ORR remained at 98%, with sCR rates higher at a median of ~2 years than at median of ~1 year (83% vs 67%)
- 2-year PFS and OS rates were 60.5% and 74.0%, respectively
- MRD negativity (at 10^{-5}) was achieved in 92% of evaluable patients
- PFS and OS was improved in patients with MRD-negativity sustained for ≥6 and ≥12 months

Cilta-cel has a manageable safety profile with no new safety signals observed with longer follow-up

These encouraging data suggest cilta-cel will be an important treatment option for patients with MM

- Cilta-cel is currently under further investigation in patients with MM in earlier-line settings, including patients with newly diagnosed MM (CARTITUDE-2[a], CARTITUDE-4[b], CARTITUDE-5[c])
- Outpatient administration of cilta-cel is being explored in these studies

Martin et al ASH 2021

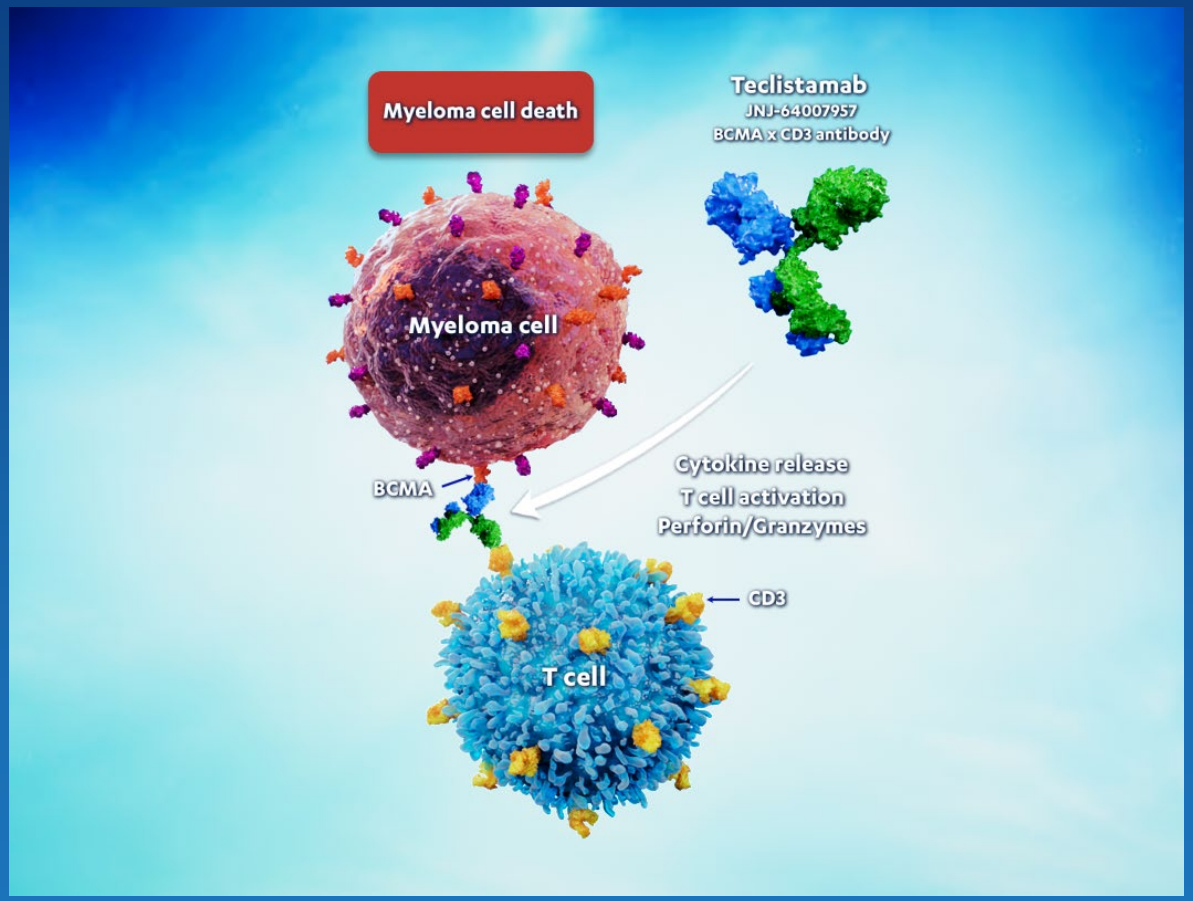
Bispecific T Cell Engagers (BiTEs) in Multiple Myeloma

	Tesclistamab Ph2 N=165	AMG-701 Ph1 N=85	REGN5458 Ph1 N=49	PF-3135 Ph1 N=30	TNB-383B Ph1 118	Talquetamab Ph1 N=157	Cevostamab Ph1 N=53
Target	**BCMA-CD3**	**BCMA-CD3**	**BCMA-CD3**	**BCMA-CD3**	**BCMA-CD3**	**GPRC5D-CD3**	**FcRH5-CD3**
Dosing Schedule	QW SC 1.5mg/kg	QW IV (0.005-18 mg)	QW→Q2W IV (3-800mg) (step up)	QW SC (80-1000µg/kg) (step up)	Q3WIV ≥ 40mg (75)	SC: 405 µg/kg QW SC: 800 µg/kg Q2W (step up)	Q3W IV 20-90mg 132-198mg (1 and 2 step up)
CRS, % Any grade Grade ≥3	71.5% 0.6%	65% 9%	38% 0	83% 0%	69% 4%	77% (405), 72% (800) 3% (800), 0% (800)	81% 1.2%
NT, % Any grade Grade ≥3	12.7% 0	Not reported	4% 0	Not reported	5%	6% 2%	14.3% 0.6%
ORR	62% (≥CR, 28.7%)	26% (≥CR, 10%)	200-800mg 75% (≥CR, 16%)	70%(≥CR 30%) 83% RP2D	≥ 40mg 60% (≥VGPR 40%)	(405): 70%(≥CR,13.3%) (800): 67% (≥CR,19%)	20-90mg, 36.1% 132-198mg, 56.7%
Median follow-up	8.0 mo responders	6.5 mo	Not reported	Not reported	4.3 mo	(405) : 9.0 mo (800) : 4.8 mo	1 step up 14.3 2 step up 6.5 mo
Median DOR	Not reached	Not reached	Not reached	Not reported	Not reached	Not reached	11.5 months (C1)
Median OS	Not reached	Not reported	Not reported	Not reported		Non reported	Not reported

Garfall et al; Harrison et al; Madduri et al Chari et al; Cohen et al ASH, ASCO 2020, Trudel et al, Krishnan et al ASH 2021; Chari et al ASH 2021; Zonder et al ASH 2021; Moreau et al ASH 2021; Kumar et al ASH 2021

Teclistamab:
A Novel BCMA × CD3 T-Cell Redirecting Bispecific Antibody

- Despite newly approved therapies for triple-class exposed patients with RRMM, unmet medical need remains high[1-2]
- Teclistamab (JNJ-64007957) is an off-the-shelf, T-cell redirecting, bispecific antibody that binds to CD3 on T cells and BCMA on plasma cells to mediate T-cell activation and subsequent lysis of BCMA-expressing MM cells
- The phase 1 portion of the MajesTEC-1 study identified the RP2D for teclistamab monotherapy: 1.5 mg/kg subcutaneous (SC) QW with step-up doses of 0.06 and 0.3 mg/kg[3]
- Here we present pivotal phase 1/2 data from the 1.5 mg/kg dose of MajesTEC-1 (NCT03145181; NCT04557098)



Moreau et al ASH 2021

MajesTEC-1: Phase 1/2 Conclusions

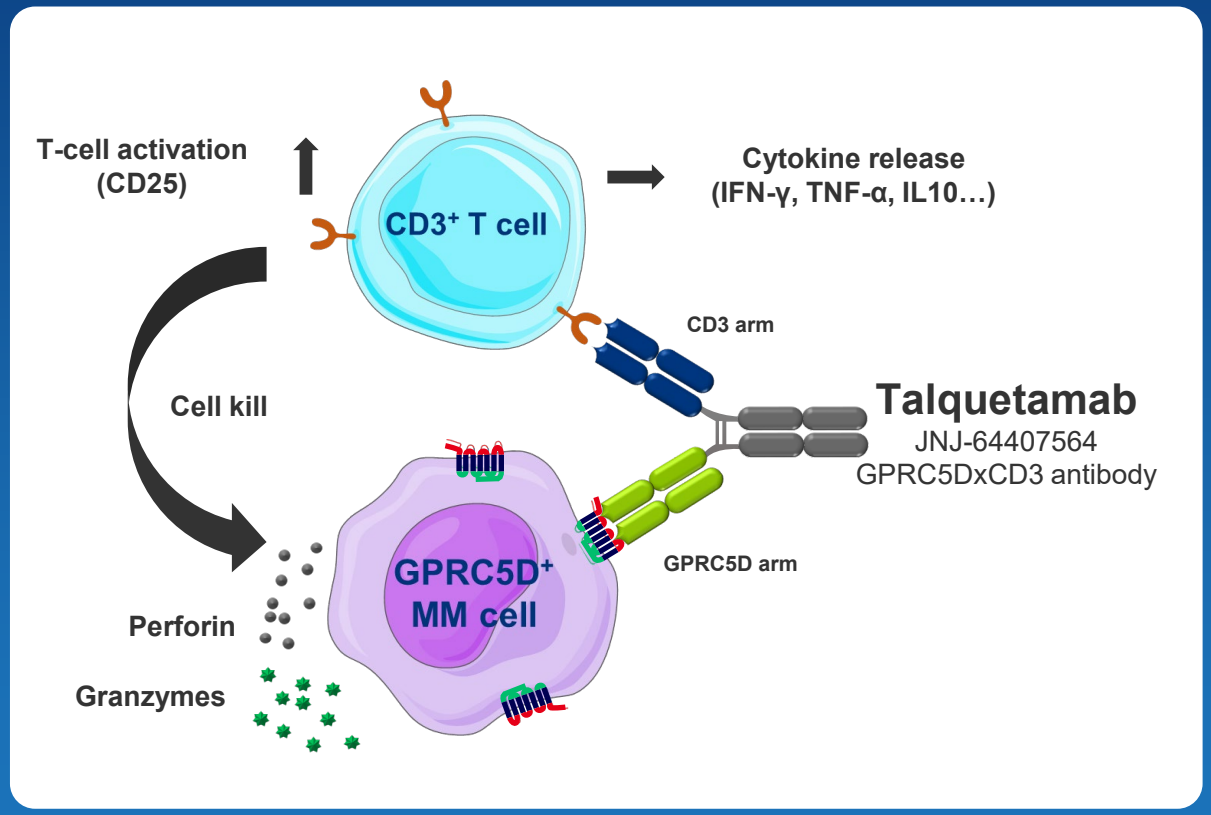
In MajesTEC-1, teclistamab was efficacious and tolerable in patients with triple-class exposed RRMM

- **62% ORR with responses that were durable and deepened over time in this heavily pre-treated population**
- **Teclistamab was well tolerated; no patients required dose reduction**
  - The most common AEs were CRS and hematologic events; CRS events were low grade, with the exception of 1 grade 3 event which resolved without discontinuation
  - ICANS events were rare, were all grade 1/2, and resolved without discontinuation
- **These data support teclistamab as a promising new, off-the-shelf, T-cell redirecting therapy targeting BCMA for patients with RRMM**
- Ongoing studies (NCT04722146, NCT04586426, NCT04108195) are evaluating teclistamab in earlier-line settings and in combination with other agents, including a phase 3 study, MajesTEC-3 (NCT05083169); data in patients with prior BCMA exposure will be presented at an upcoming congress

Moreau et al ASH 2021

Talquetamab: a GPRC5D × CD3 Bispecific Antibody

- GPRC5D is highly expressed on MM plasma cells and to a lesser extent in normal tissues, making it a promising target for MM therapy[1-5]
- Talquetamab is a first-in-class antibody that binds to GPRC5D and CD3 receptors, mediating T cell recruitment, activation and subsequent lysis of GPRC5D+ MM cells[6]
- In the ongoing, phase 1, first-in-human study of talquetamab in patients with RRMM (MonumenTAL-1; NCT03399799), the first RP2D was identified as a weekly SC dose of 400 µg/kg[a,7–8]
- Here we present
  - Updated data from patients treated at the first RP2D[a]
  - Initial results from patients treated at a second RP2D of 800 µg/kg Q2W



Krishnan et al ASH 2021

MonumenTAL-1 Phase 1 Conclusions

- **Talquetamab, a novel, off-the-shelf, T-cell redirecting, bispecific antibody that binds to GPRC5D and CD3, appears tolerable in heavily pretreated patients with RRMM**
  - 800 µg/kg SC Q2W dosing has comparable efficacy and safety to 405 µg/kg SC QW dosing
  - No new safety signals were identified at either RP2D
- **Longer follow-up supports the encouraging efficacy of QW or Q2W doses of talquetamab, with a 67–70% ORR that is maintained in triple-class and penta-refractory patients**
  - Responses were durable and deepened over time
- **Pharmacokinetic and pharmacodynamic data support QW and Q2W dose schedules**
- **A phase 2 expansion study of talquetamab at the RP2Ds[a] is in progress (NCT04634552)**
- **Additional ongoing phase 1/2 studies are evaluating talquetamab in combination with other agents (NCT04586426; NCT04108195; NCT05050097)**

Krishnan et al ASH 2021

TRIMM-2: Talquetamab and Daratumumab Conclusions

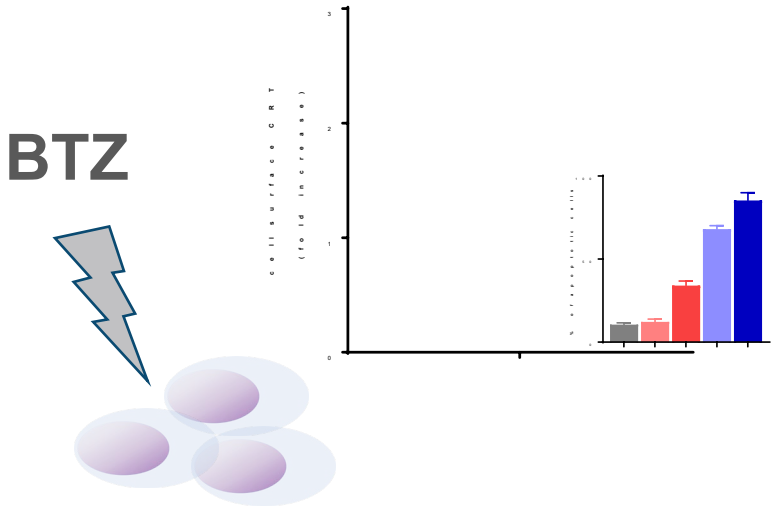
- **The combination of talquetamab + daratumumab appears tolerable, with no overlapping toxicity**
  - Safety profiles appear consistent with each agent given as a monotherapy and no new AEs were observed
  - 55% of patients experienced CRS, all grade 1 and 2, with median time to onset of 2 days and 2 days duration
- **Preliminary efficacy data suggest a promising ORR (77–85%) in these heavily pretreated patients**
  - Responses were observed in both CD38–exposed and –refractory patients
  - Responses were durable and appeared to deepen over time, with the majority of patients remaining on treatment
- Tal-mediated induction of cytotoxic T cells (CD38+/CD8+) in the presence of dara supports the rationale for this synergistic combination regimen
- **These data support tal + dara as a novel immunotherapy-based approach for the treatment of patients with MM**

Chari et al ASH 2021

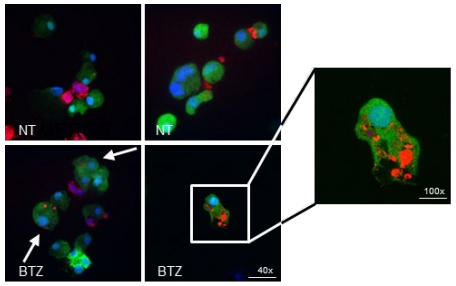
Bortezomib (BTZ) Triggers Anti-MM Immune Response (Immunogenic Cell Death)

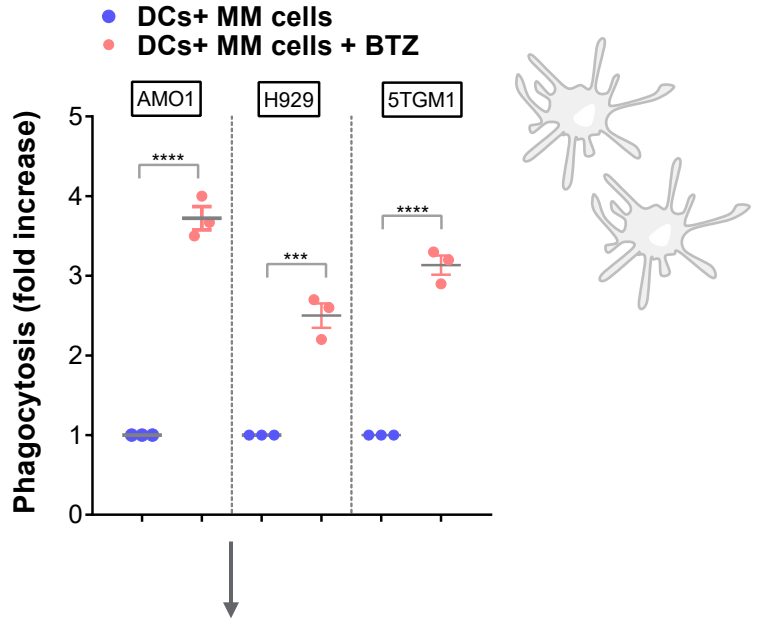
1. MM cells expose CALR on cell surface

BTZ

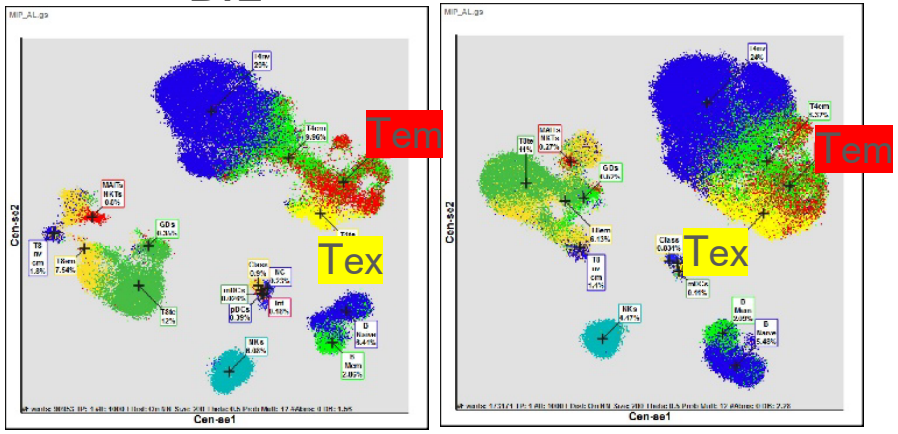


2. Dendritic cells become functionally mature

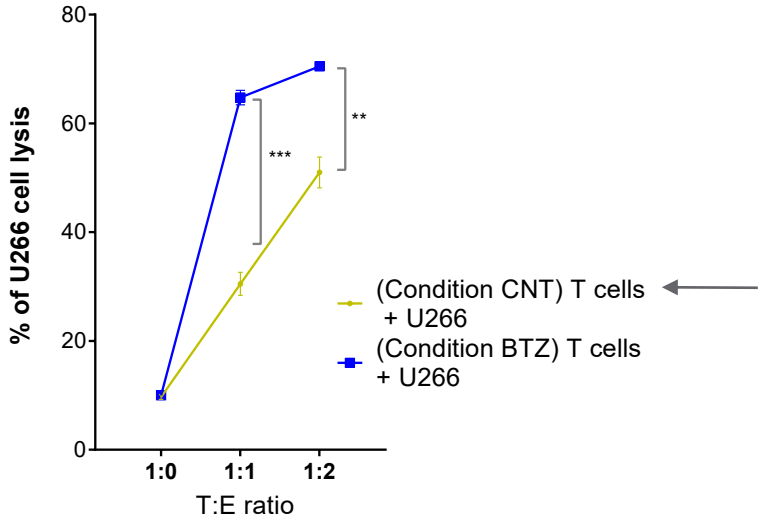




3. T cells are primed against MM



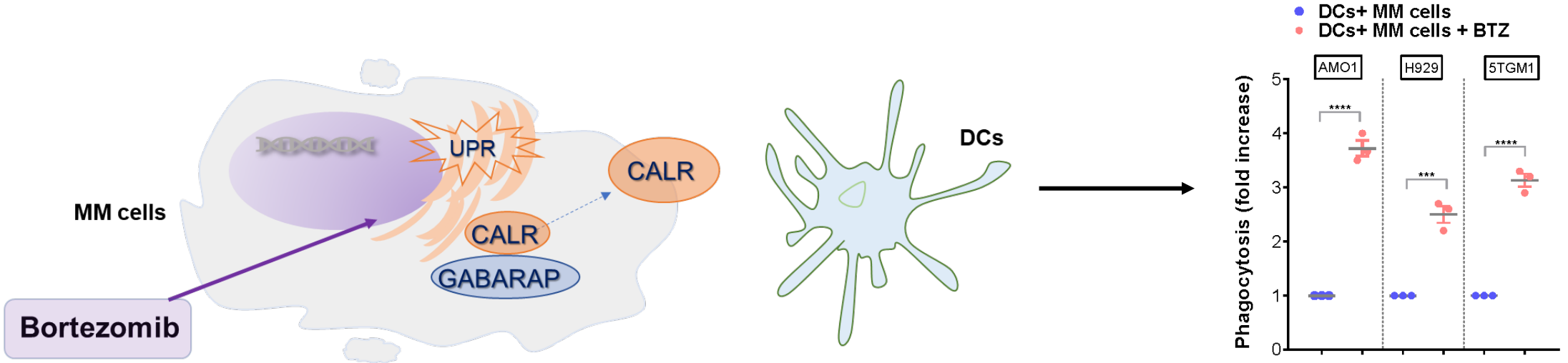
4. MM cell lysis



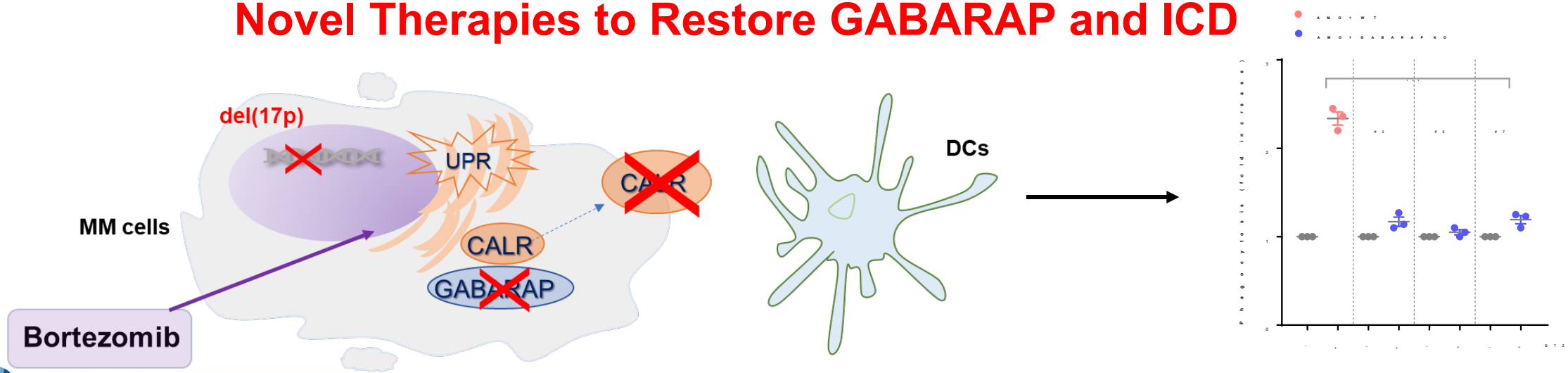
Gulla et al, Blood Cancer Discovery, in press

Dana-Farber Cancer Institute

Loss-of-function of GABARAP (on 17p) in High Risk MM Abrogates Induction of ICD



Novel Therapies to Restore GABARAP and ICD

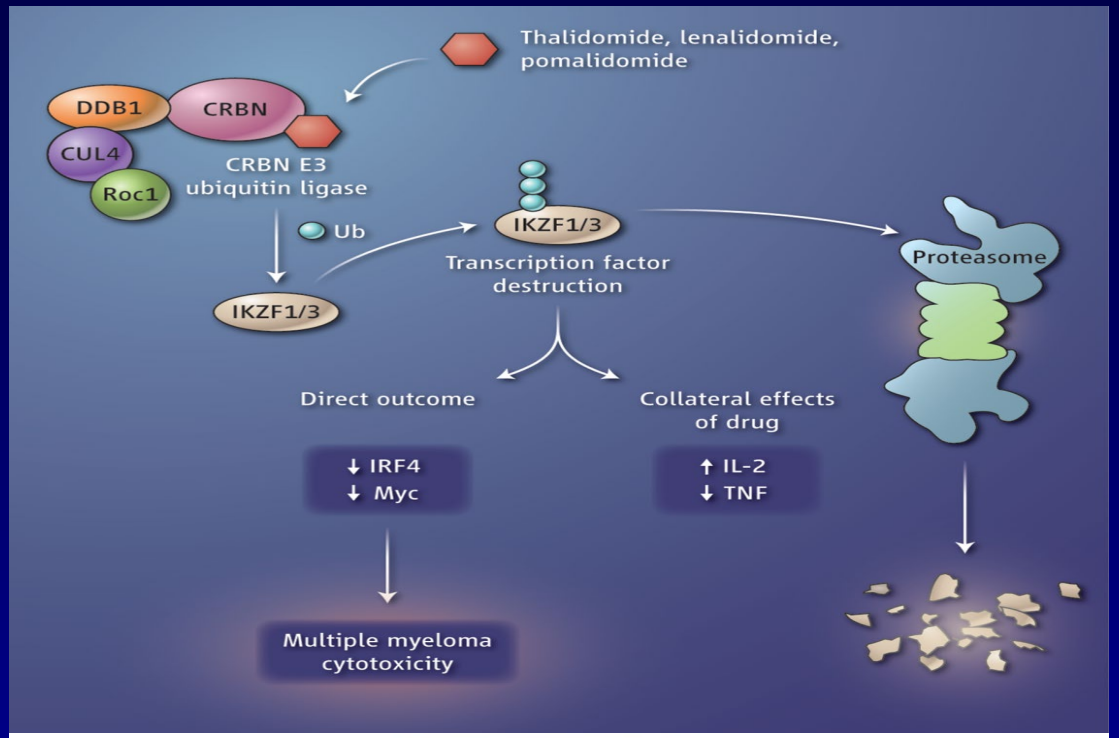


Gulla et al, ASH 2021

Immunomodulatory Drugs Target Cereblon in Tumor and Microenvironment

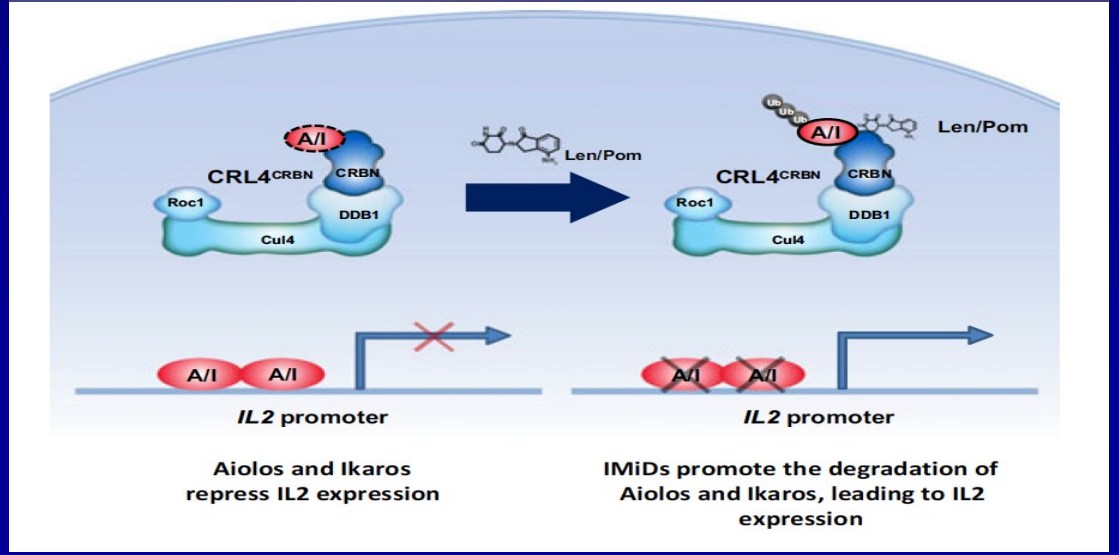
CELMoDs: increased CRBN affinity, CC220, CC92480) responses In len/pom resistant MM (Lonial et al, Richardson et al ASCO, ASH 2019, 2020, 2021)

CC220: ORR 26%, (97% triple class refractory) 92480/Bort/Dex: ORR 73% (47% pom, 37% Dara, 21% triple class refractory)



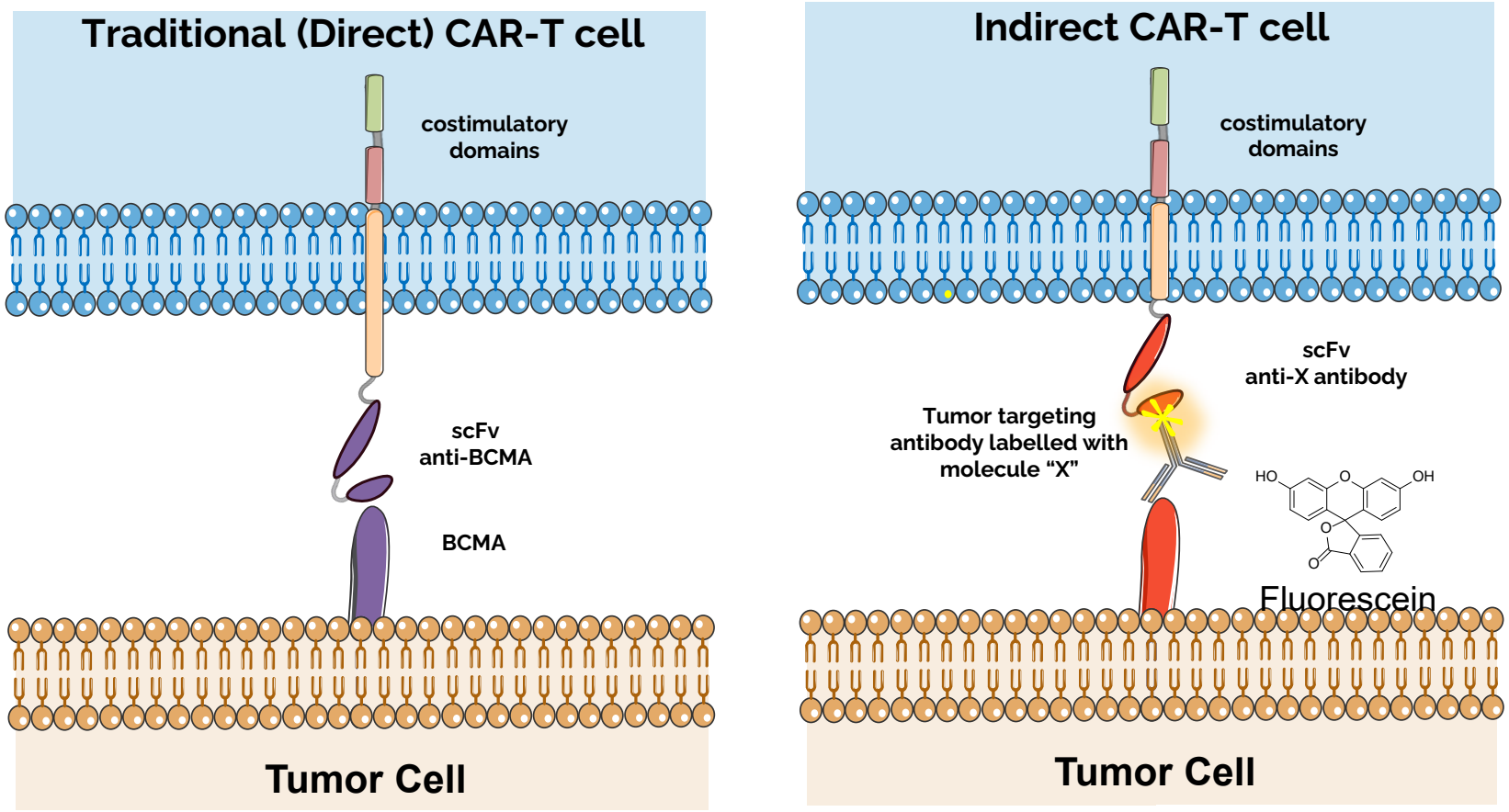
Kronke et al, Science, 2014

Lu et al, Science, 2014



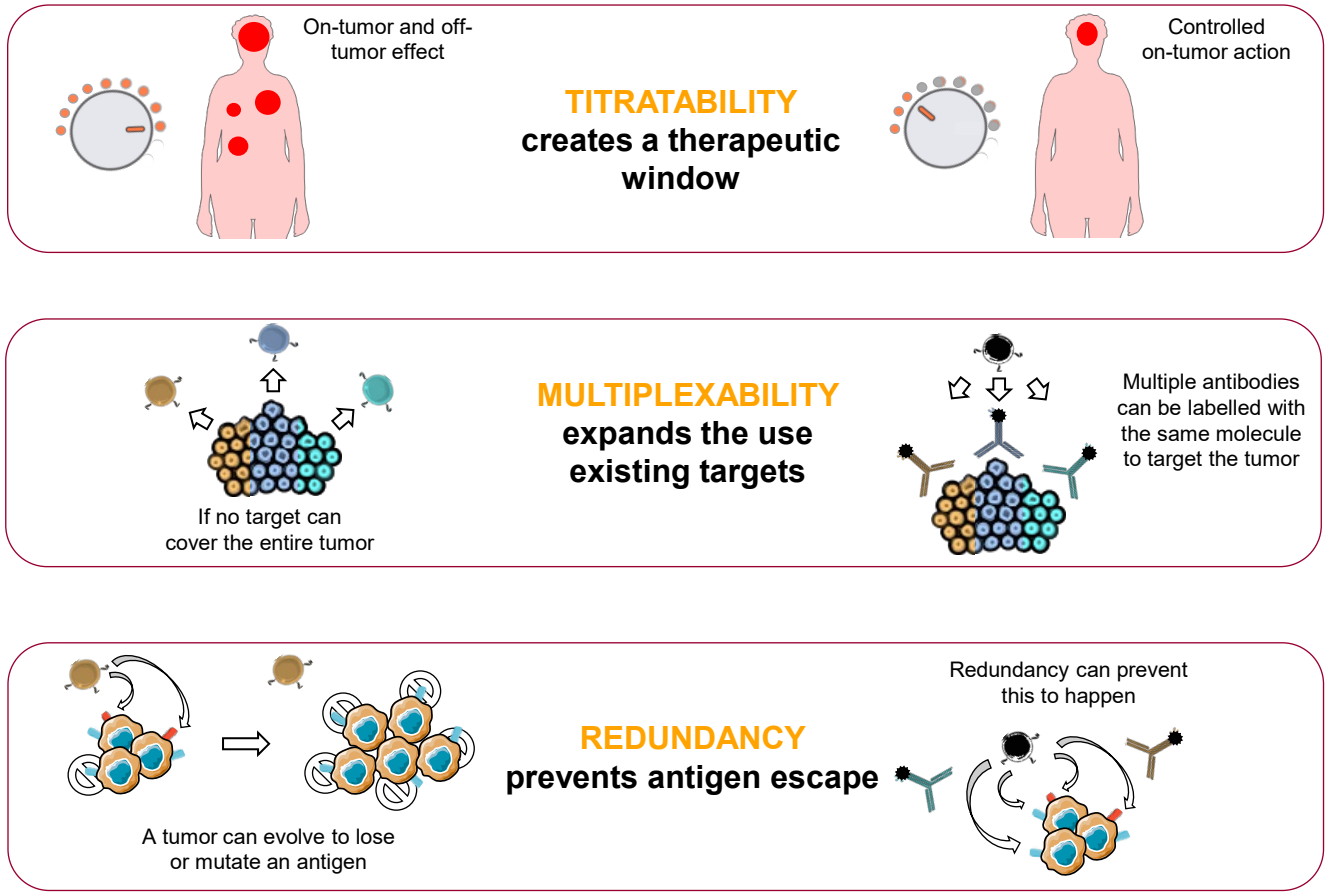
Gandhi AK et al. Brit J Haematol, 2014;164: 811-21.

BAT-CAR: Binary Activated T Cell with Chimeric Antigen Receptor



Alberto Nobili, PhD and Carl Novina, MD PhD

BAT CARs Target Limitations of CAR T Cells



Alberto Nobili, PhD and Carl Novina, MD PhD

Summary and Conclusions

Combinations incorporating CD 38 Ab now used to treat all newly diagnosed MM, including HR disease, i.e. RVD-Dara, RD-Dara

Choice of therapy for relapsed MM dependent on clinical features and prior therapy.

Triplets achieve increased extent and frequency of response, PFS, and OS in relapsed MM.

Novel targeted/immune approaches include BCMA directed immunotoxin, venetoclax, bispecific T cell engagers, and CAR T cells.

Future Directions

Combination PI, IMiD, Dex, CD38MoAb will achieve high rates MRD negativity in NDMM, including high risk MM

BCMA targeted BiTEs and CAR T cells, will then be compared with ASCT to induce long term MRD-with memory anti-MM immune response

Novel uses of known classes of active agents:
Proteasome inhibitors to trigger anti-MM immune response
More potent immunomodulatory drugs

Combination novel immunotherapies to enhance response, overcome resistance mechanisms, and improve therapeutic index: BiTEs with CD38 MoAbs

Novel adoptive immunotherapy: novel CAR T cell targets (GPRC5D) and BAT CARs

Long term disease-free survival and potential cure of MM will be achieved with combination targeted and immune therapies to both achieve MRD negativity and restore host memory anti-MM immunity. These patients will then be free of disease and off all therapy..