Actualización en el tratamiento del mieloma múltiple con anticuerpos biespecíficos, anticuerpos conjugados y CAR-T cells

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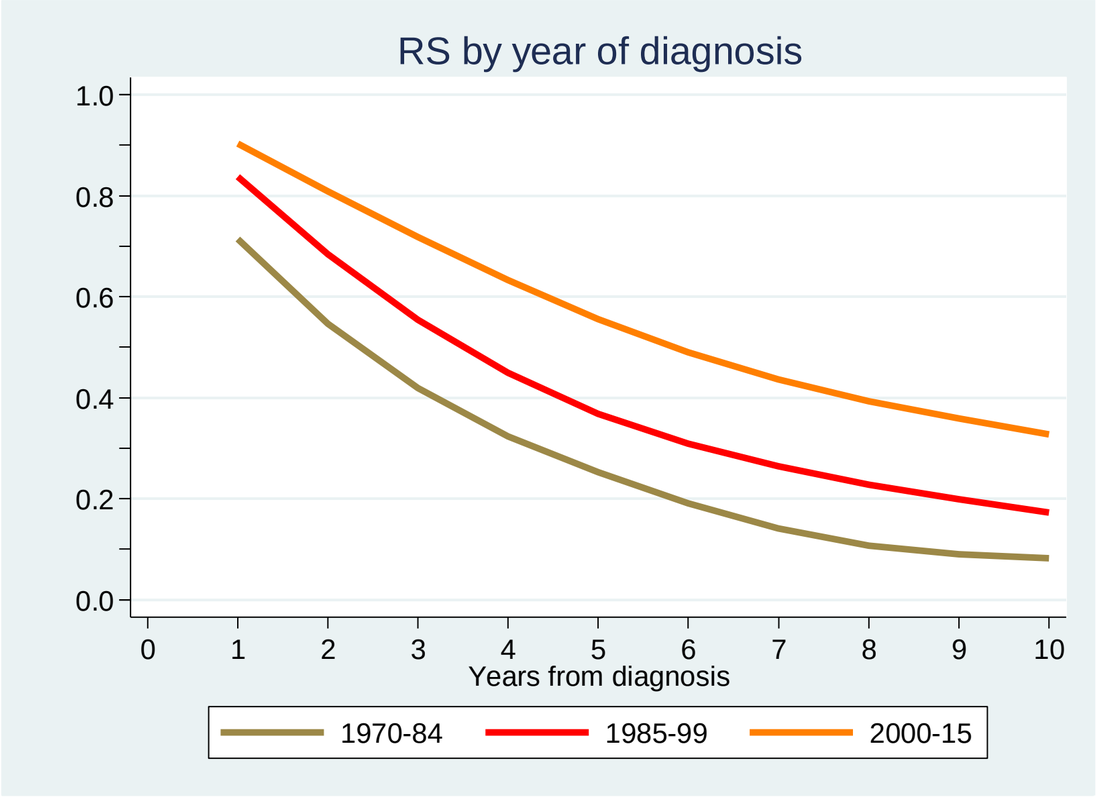
Inmunoterapia & Hemopatías
Quinta edición

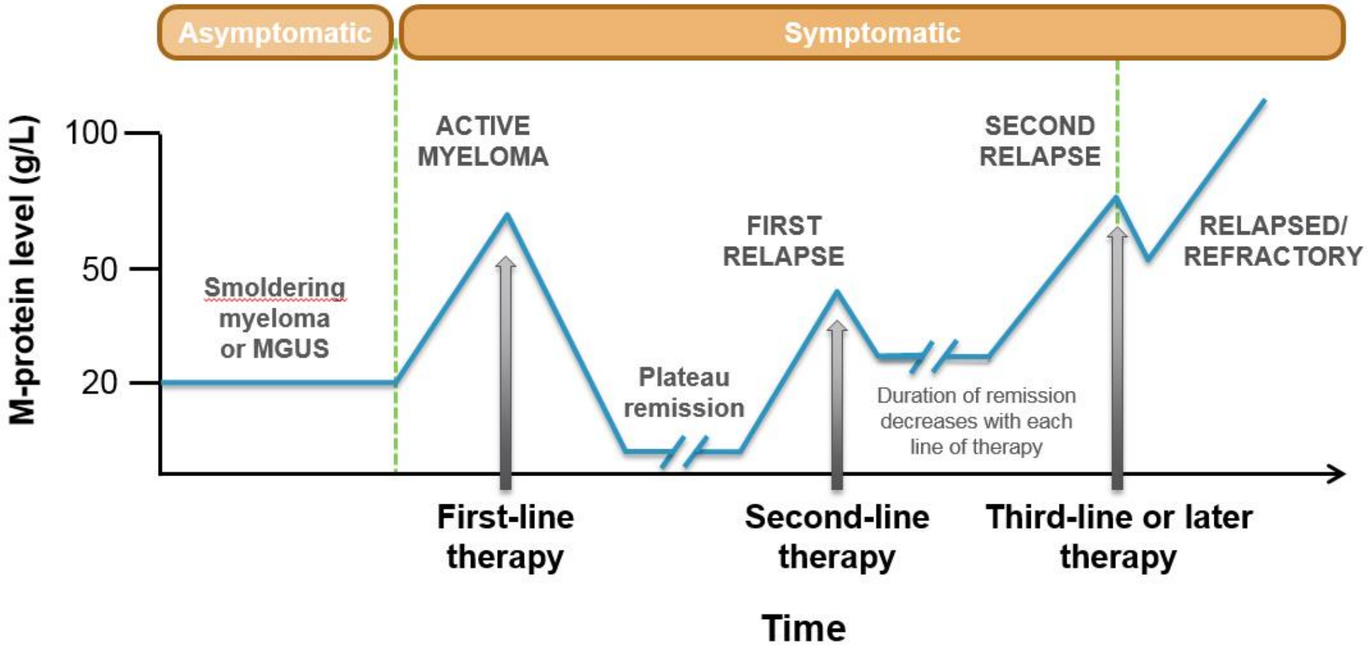
Disclosures

- Advisory boards: *Janssen, BMS, Amgen, Pfizer, Sanofi*
- Honoraria: *Amgen, Janssen, BMS, GSK, Sanofi*
- Grants: *BMS, Janssen, Amgen, GSK*

Multiple myeloma remains an almost always incurable disease

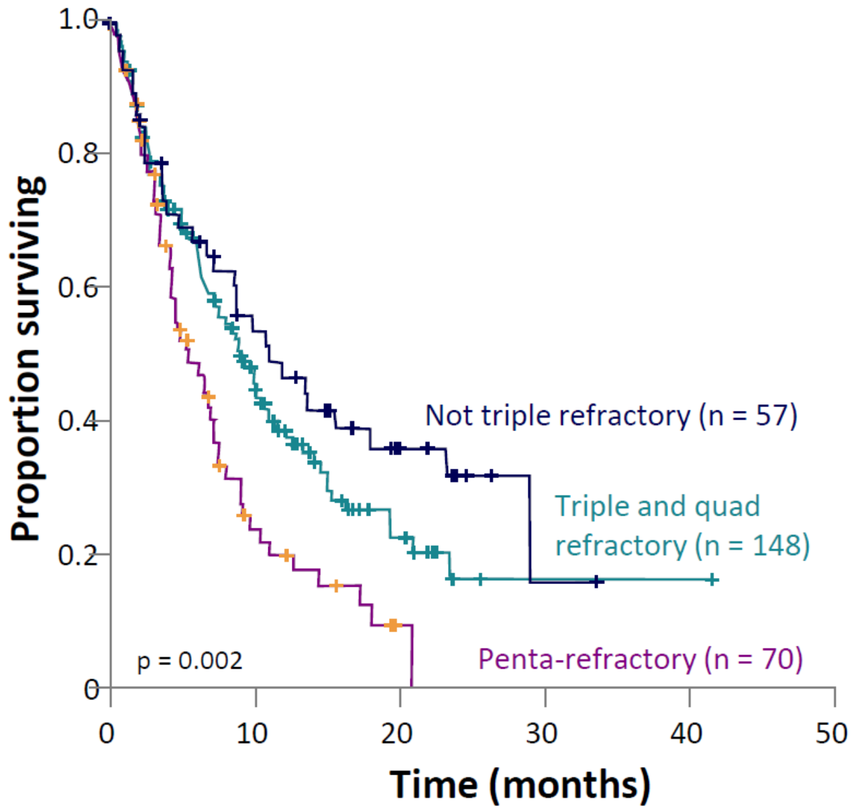


Rodriguez-Lobato *et al*. BJH 2021

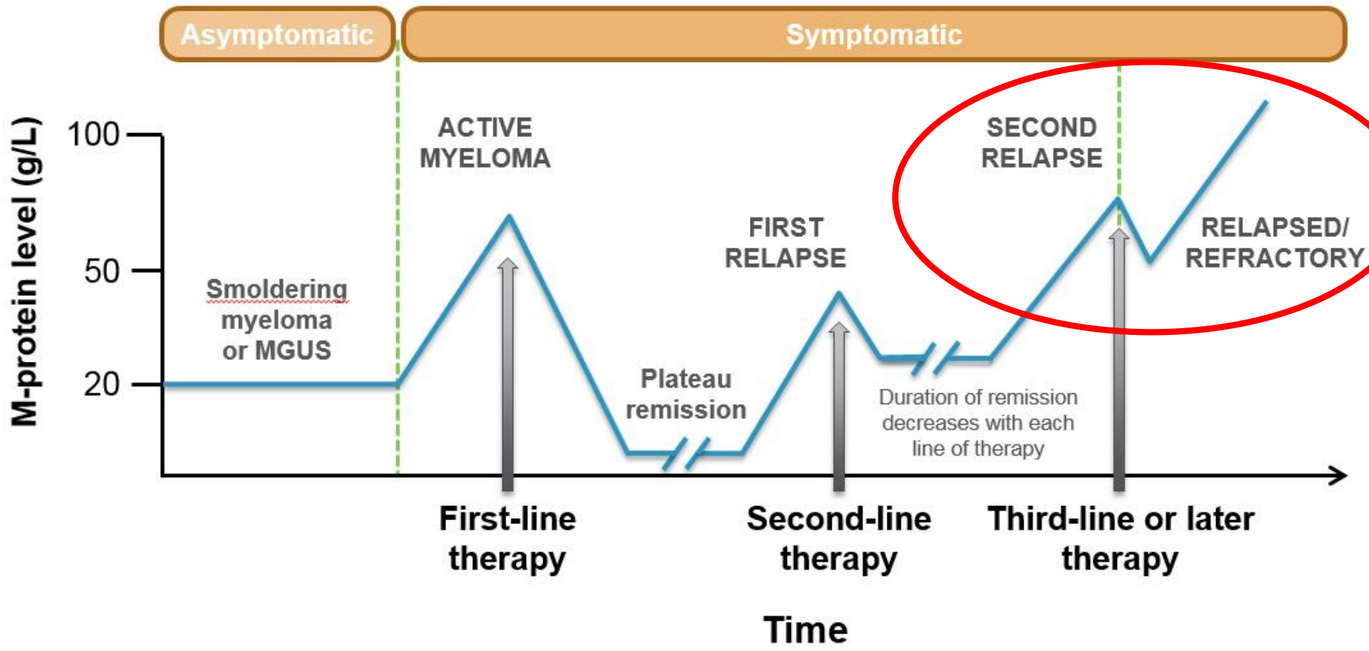


Kumar *et al*. Nat Rev Dis Primers 2017

Multiple myeloma (MM) remains an almost always incurable disease

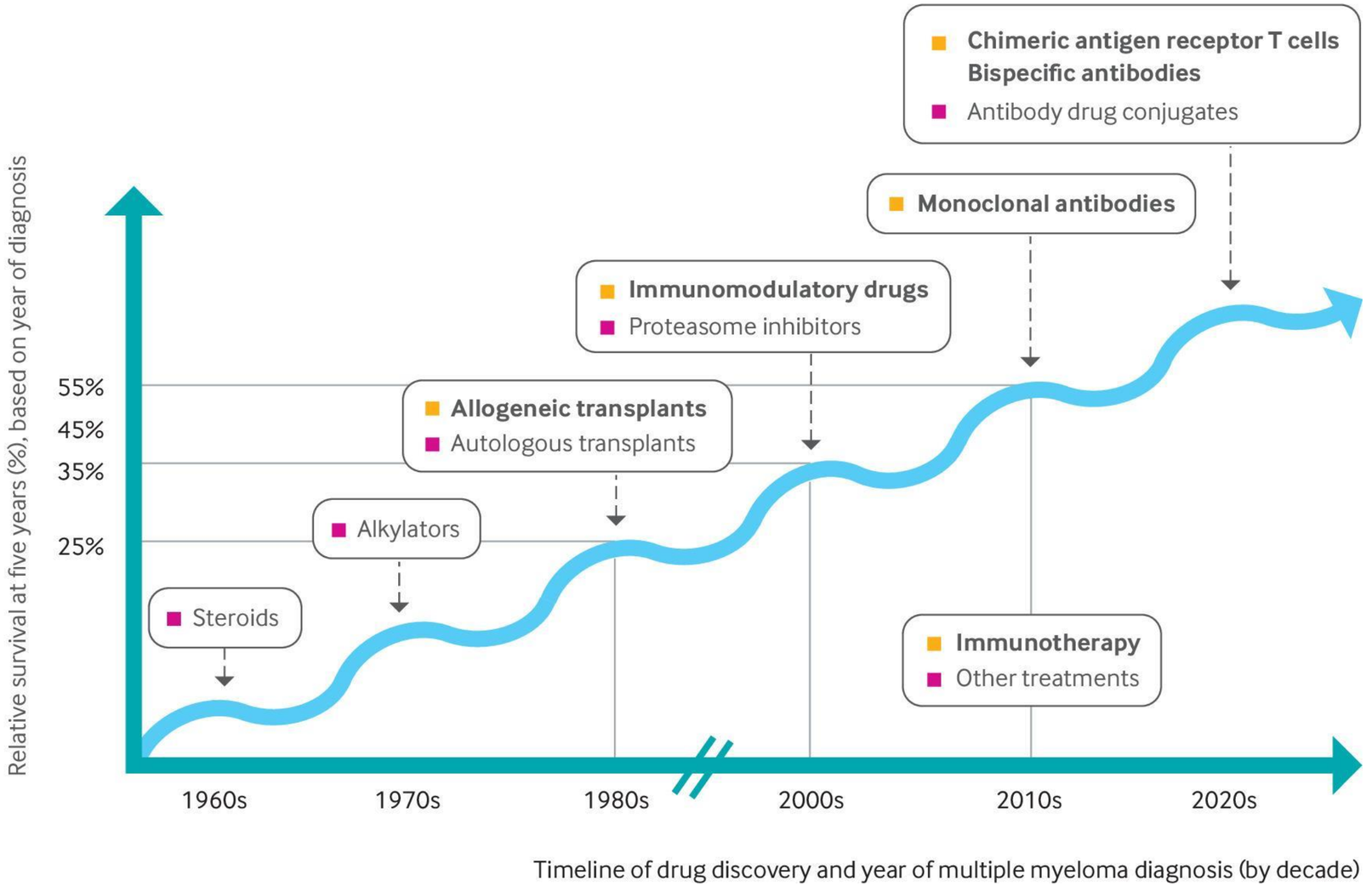


Gandhi *et al*. Leukemia 2019



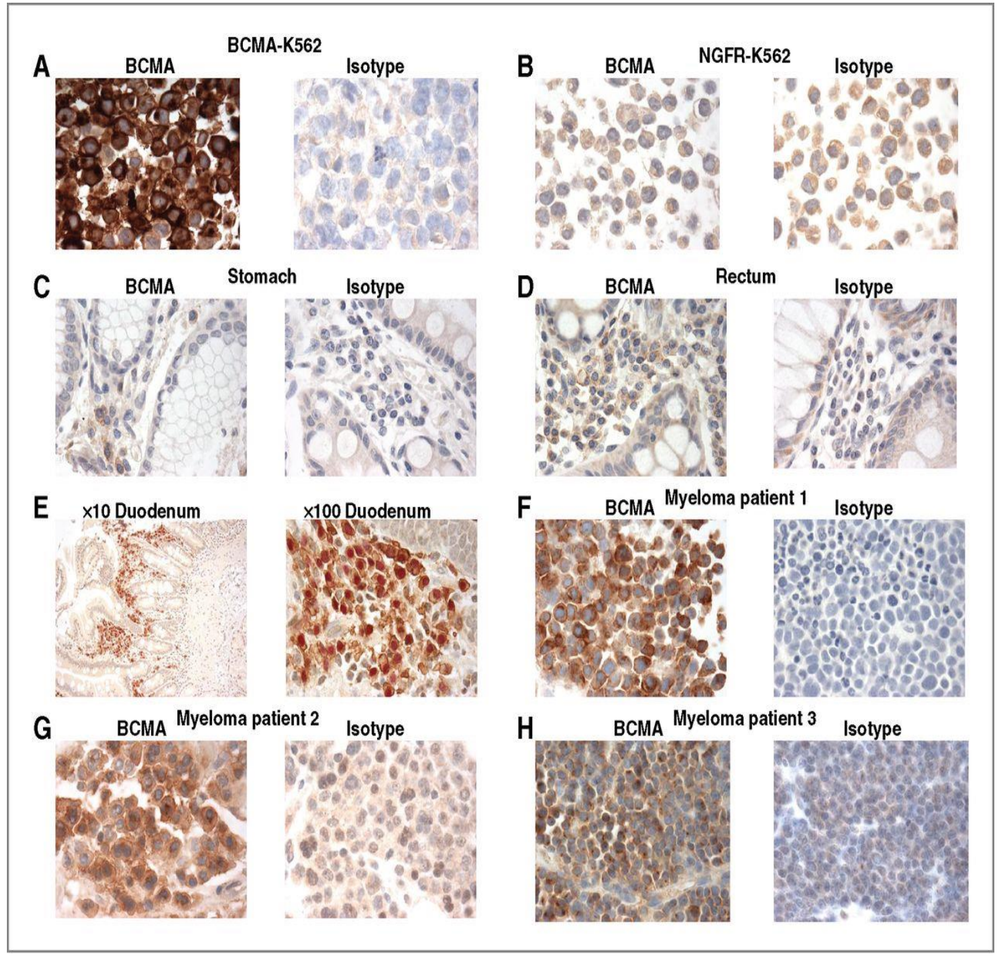
Kumar *et al*. Nat Rev Dis Primers 2017

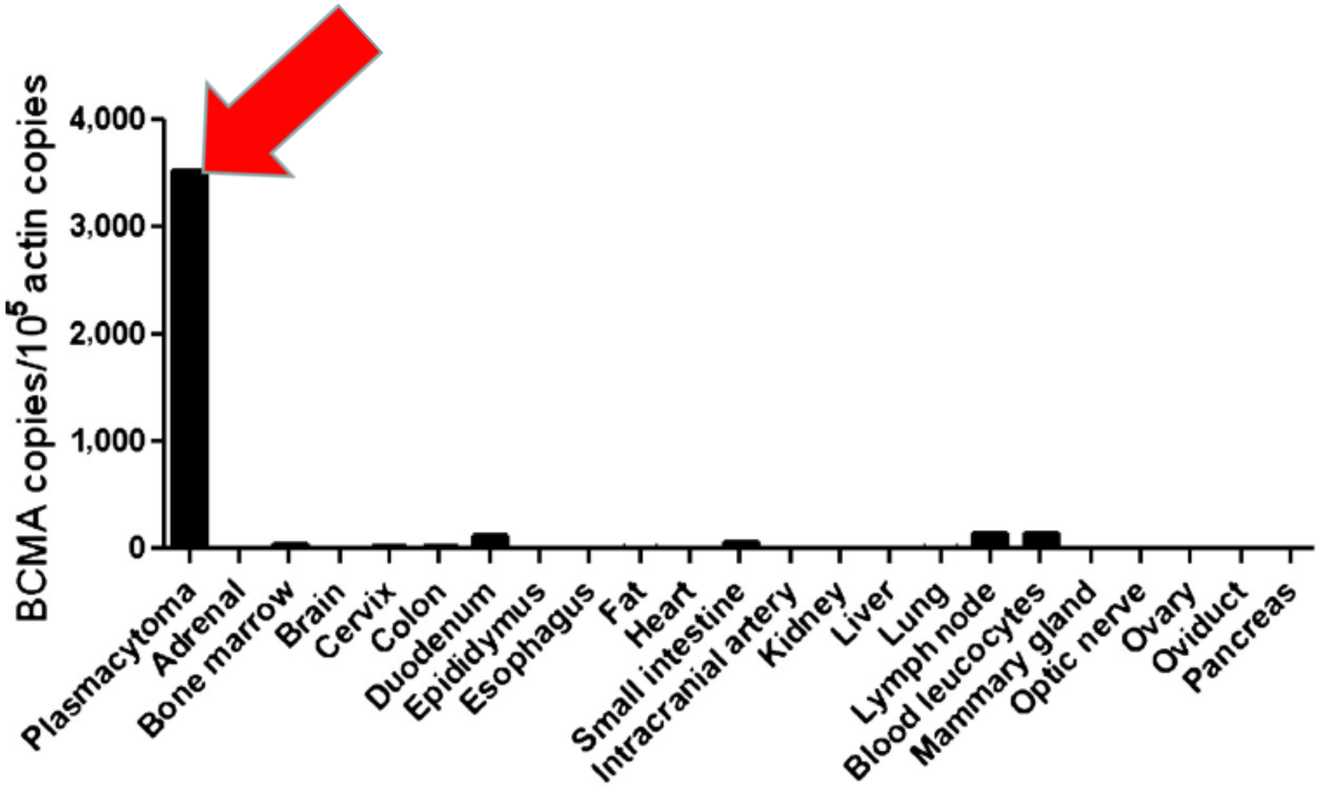
The impact of immunotherapy in multiple myeloma (MM)



Shah and Mailankody. BMJ 2020

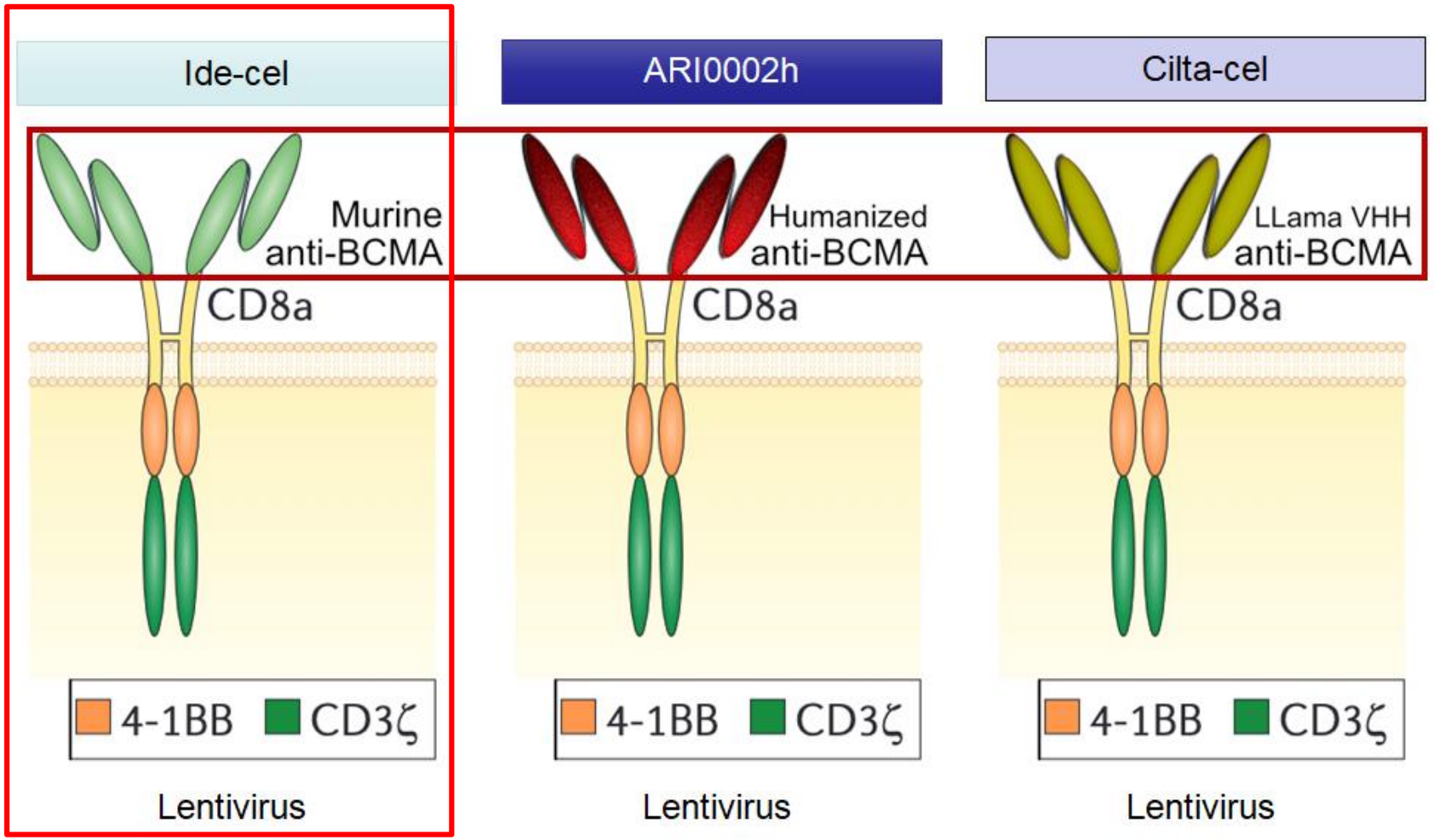
BCMA is an optimal target for immunotherapy in MM





Carpenter RO *et al*. CCR 2013

CAR-T against BCMA in MM



Idecabtagene vicleucel

Ciltacabtagene autoleucel

BCMA CAR T Cell Therapy: KarMMa study: Idecabtagene vicleucel (ABECMA; ide-cel; bb2121) approved by FDA/EMA 2021

- Open-label, single arm study: N=140
- ≥ 3 prior therapies (including an IMiD, a PI and an anti-CD38 antibody); median: 6 lines of prior therapy
- 94% of patients refractory to anti-CD38 antibody; 84% triple-refractory, EMD: 39%
- Median follow-up: 11.3 months

Efficacy

	Ide-cel Treated Population			
	150 x 10^6 CAR+ T cells (N=4)	**300 x 10^6 CAR+ T cells (N=70)**	**450 x 10^6 CAR+ T cells (N=54)**	**150–450 x 10^6 CAR+ T cells (N=128)**
ORR, n (%)	2 (50.0)	48 (68.6)	44 (81.5)	94 (73.4)
CR/sCR, n (%)	1 (25.0)	20 (28.6)	19 (35.2)	40 (31.3)
Median DoR, months	---	9.9	11.3	10.6
Median PFS, months	---	5.8	11.3	8.6

Median DOR and median PFS are not reported for the 150 x 10^6 CAR+ T cells dose group due to the small number of evaluable patients

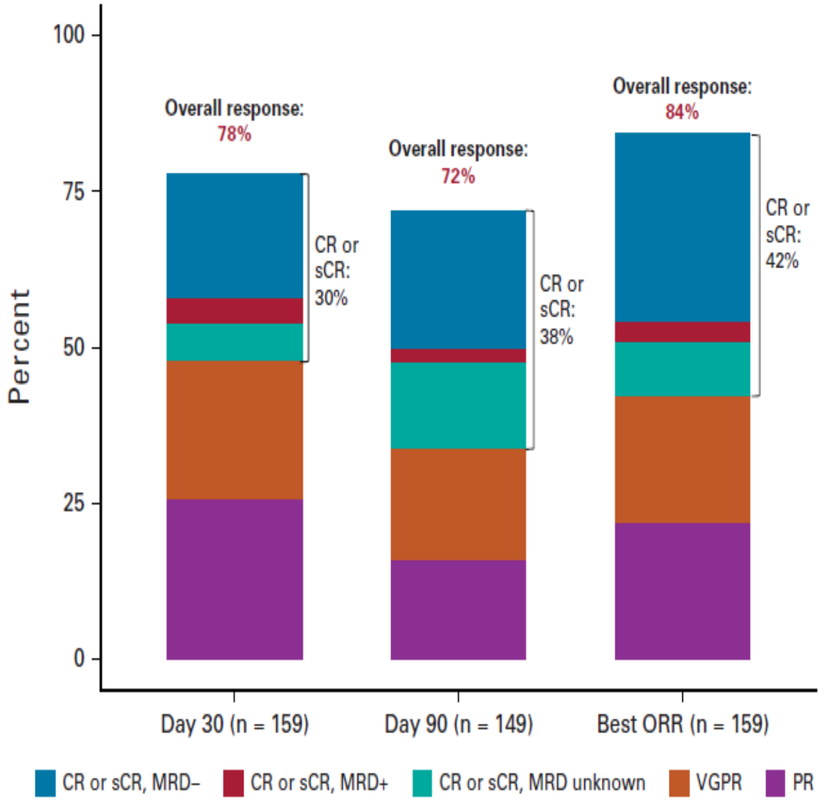
- Grade ≥ 3 CRS: 5.5%
- Grade ≥ 3 investigator identified neurotoxicity events: 3.1%

In the subgroup of pts. achieving a CR: PFS > 20 m.

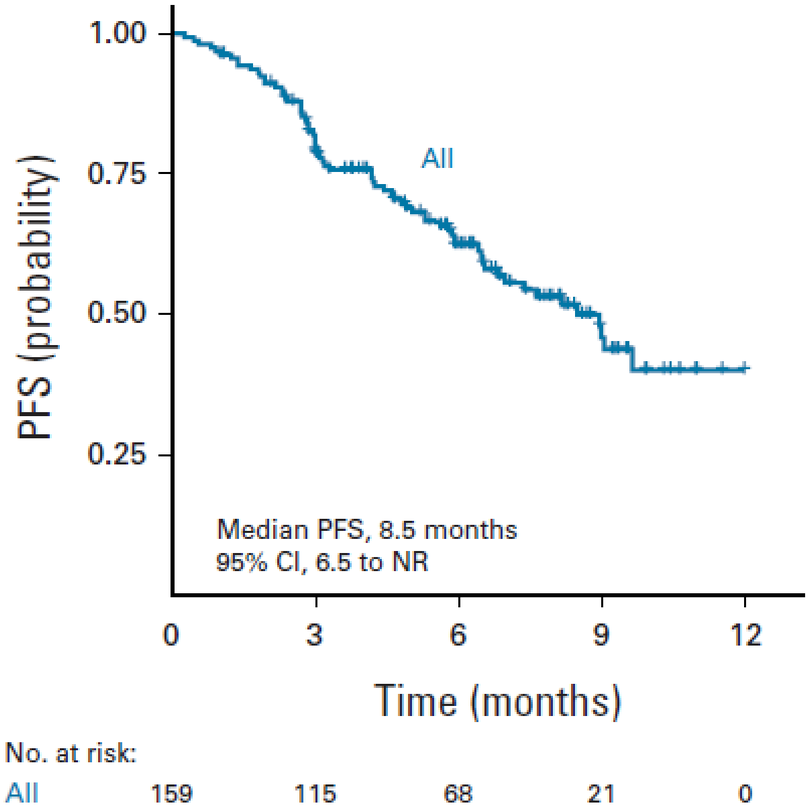
Munshi N *et al*. NEJM 2021

Ide-cel in real world experience

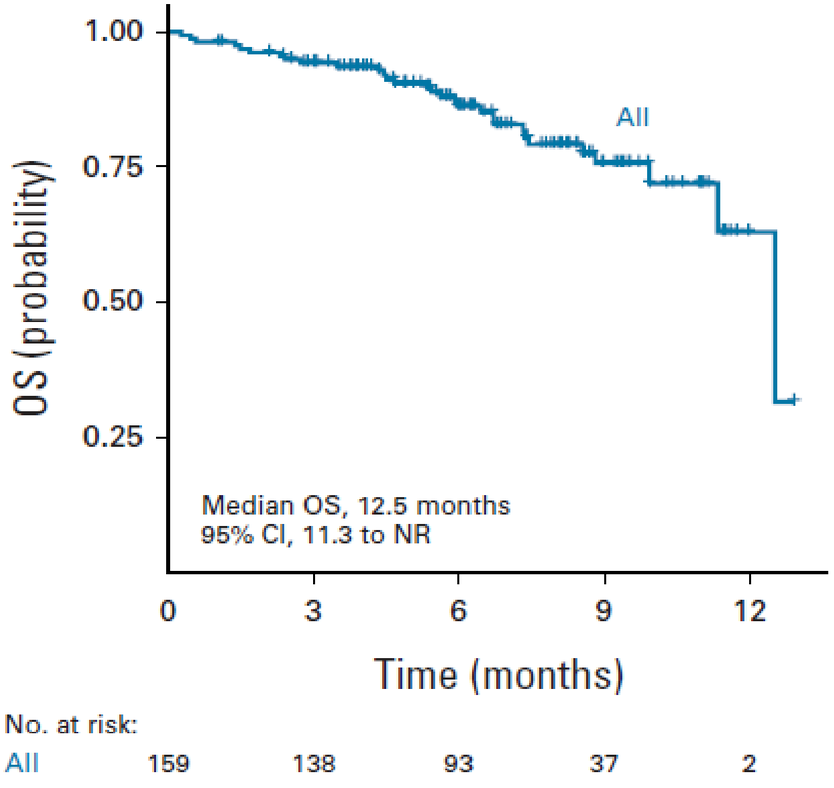
ORR : 84%



Med PFS : 8.5 mos

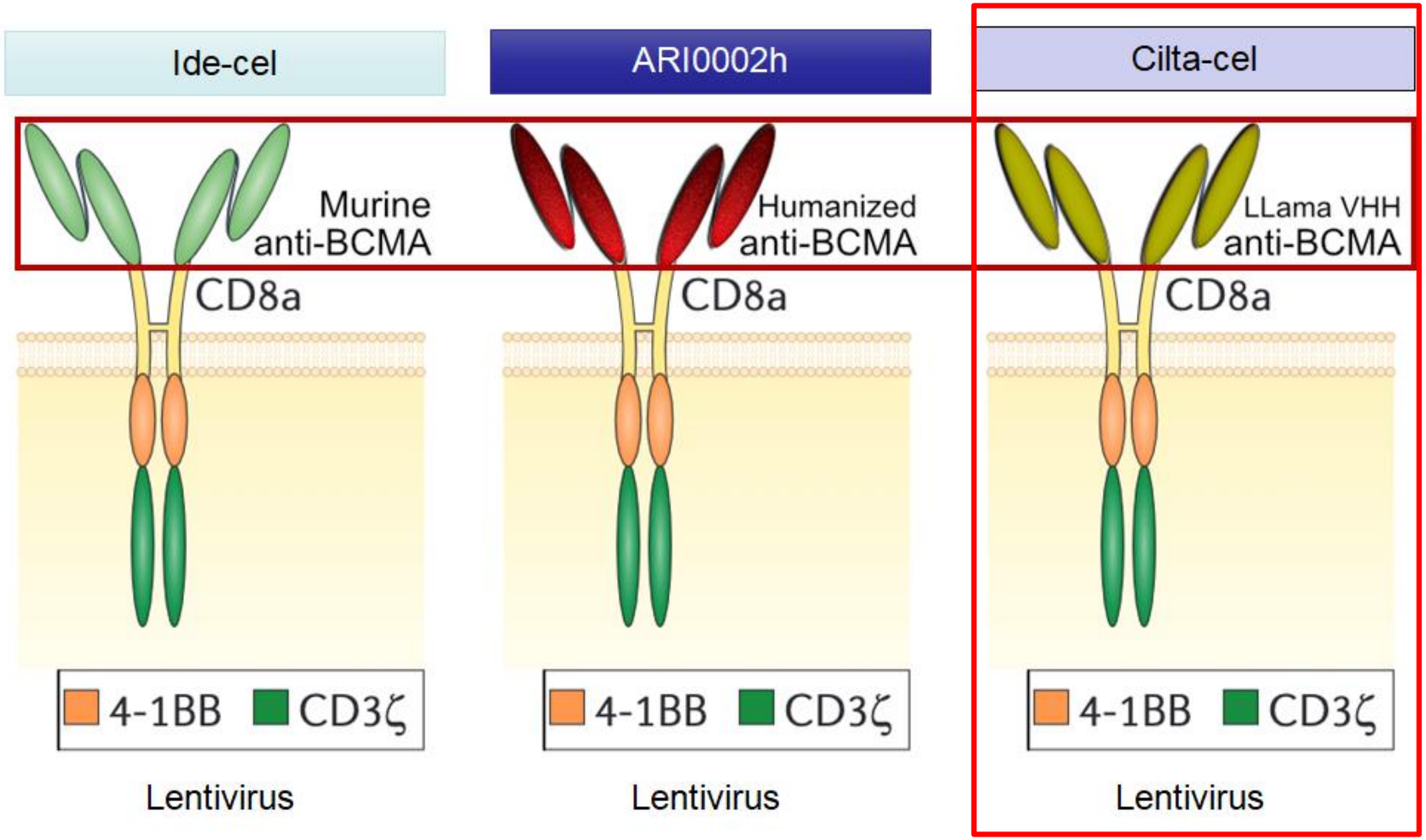


Med OS : 12.5 mos



Hansen *et al*. JCO 2023

CAR-T against BCMA in MM

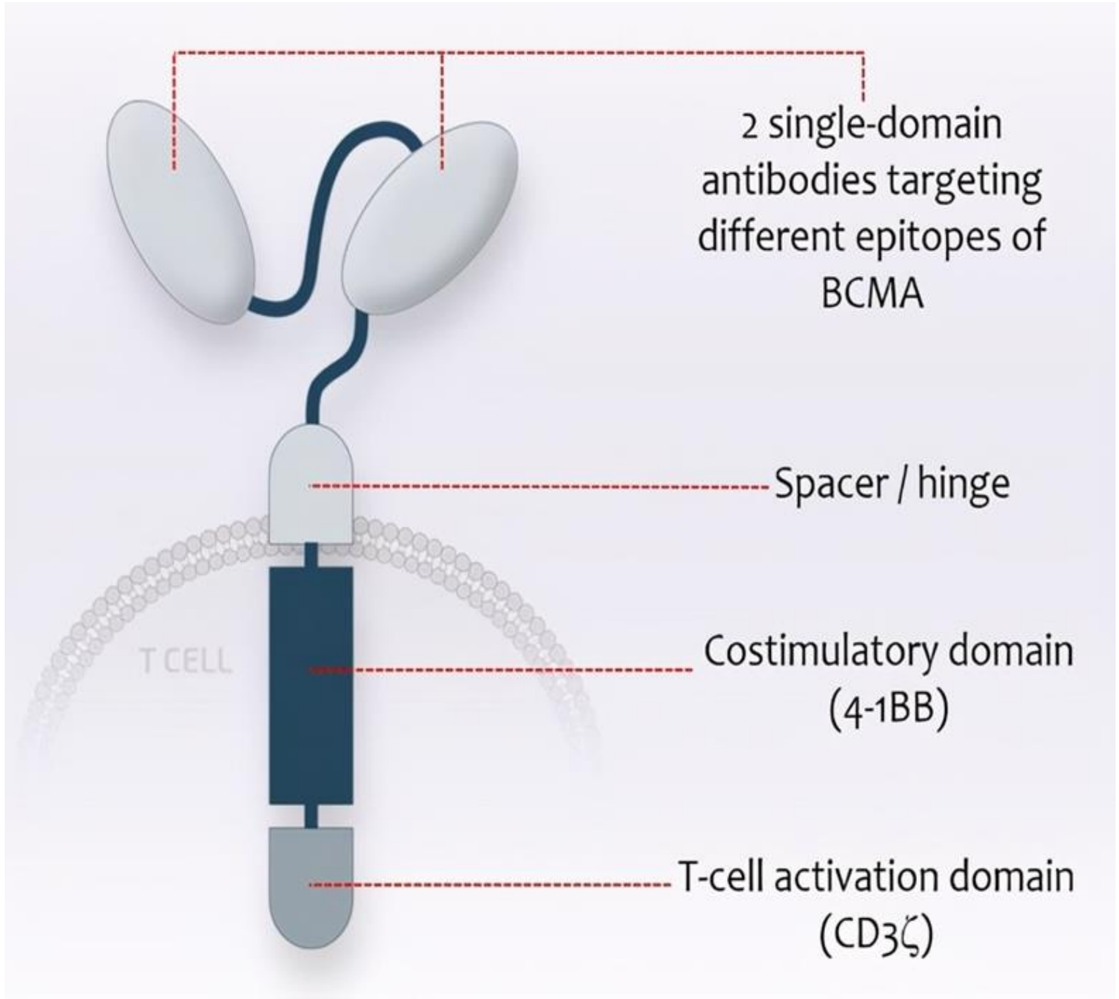


Idecabtagene vicleucel

Ciltacabtagene autoleucel

Cilta-Cel CAR T Cell Product targeting BCMA with 2 target domains

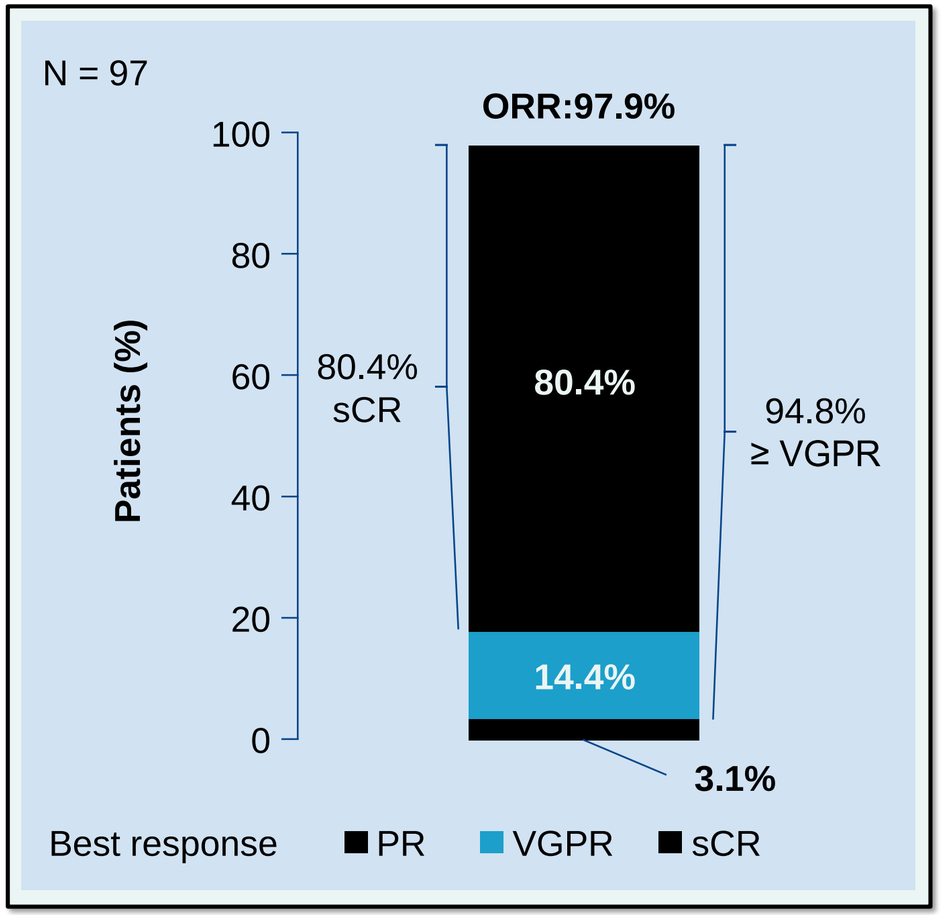
BCMA-directed CAR T Cell Therapy with Cilta-Cel



Characteristic	
Prior lines of therapy, median (range)	6.0 (3–18)
Prior lines of therapy, n (%)	
3	17 (17.5)
4	16 (16.5)
≥5	64 (66.0)
Previous stem-cell transplantation, n (%)	
Autologous	87 (89.7)
Allogeneic	8 (8.2)
Triple-class exposed,[c] n (%)	97 (100)
Penta-drug exposed,[d] n (%)	81 (83.5)
Triple-class refractory[c]	85 (87.6)
Penta-drug refractory[d]	41 (42.3)
Refractory status, n (%)	
Carfilzomib	63 (64.9)
Pomalidomide	81 (83.5)
Anti-CD38 antibody	96 (99.0)
Refractory to last line of therapy, n (%)	96 (99.0)
EMD:	**13 (13.4)**

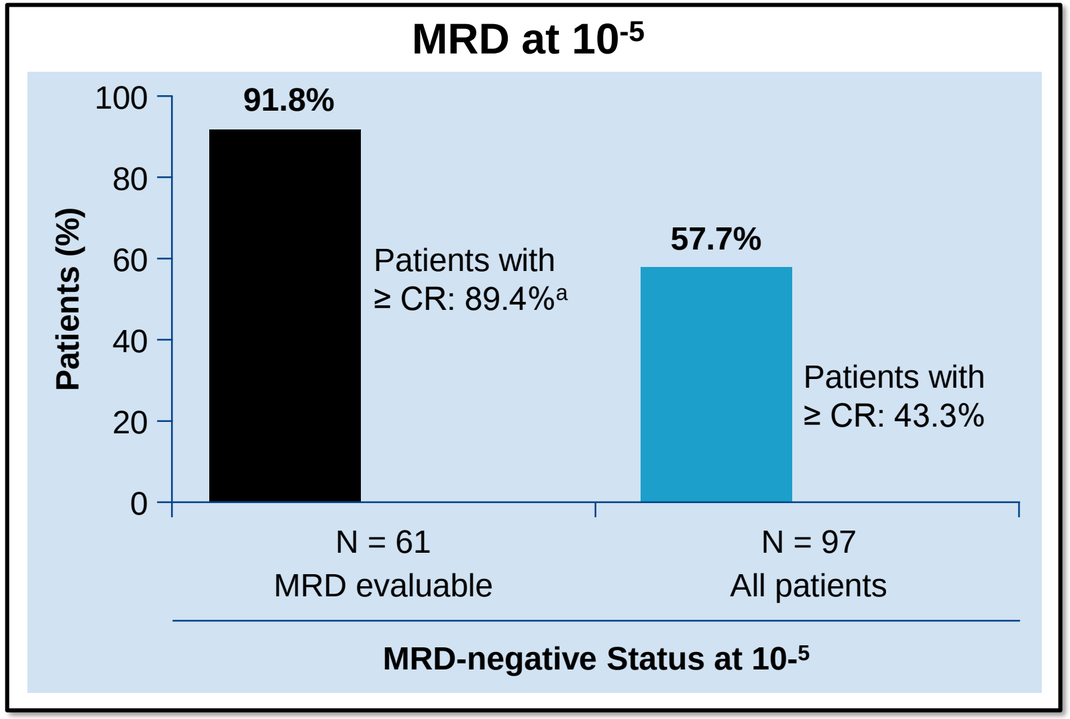
Berdeja JG, et al. Lancet 2021
Usmani S, et al. ASCO 2022

CARTITUDE-1: Overall response



Median time to first response 1 month (range: 0.9–10.7)

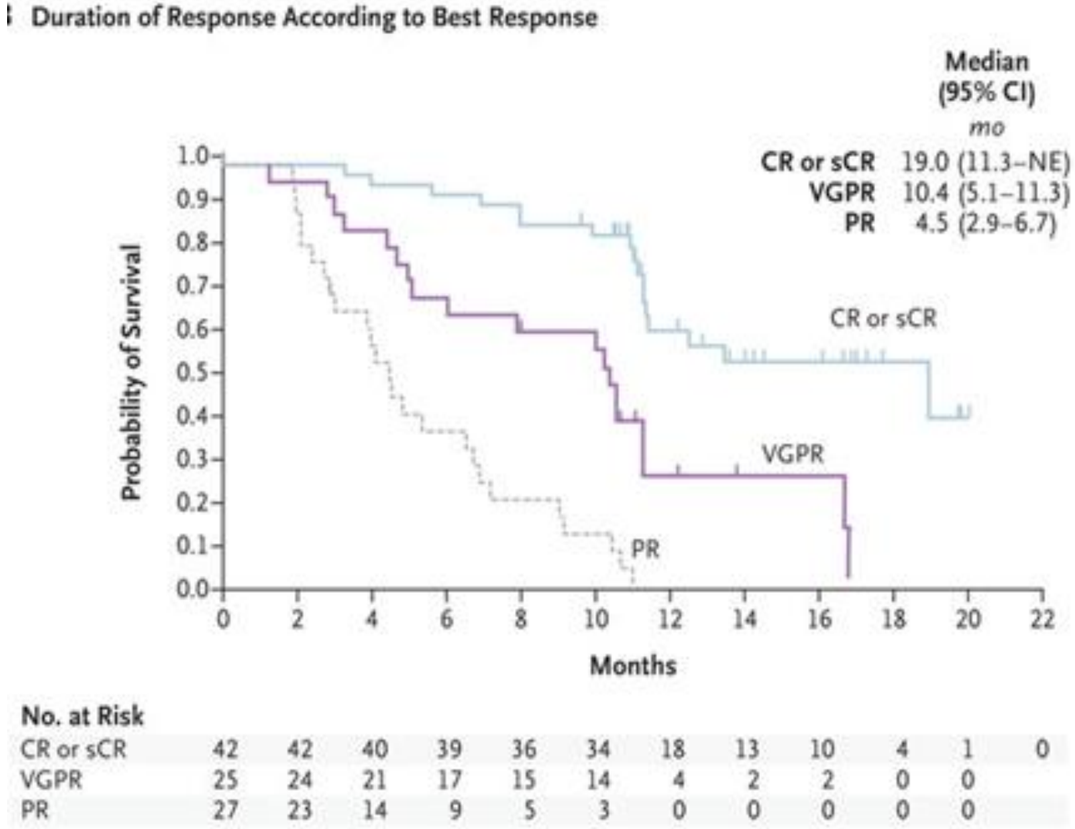
Median time to best response 2.6 months (range: 0.9–15.2)

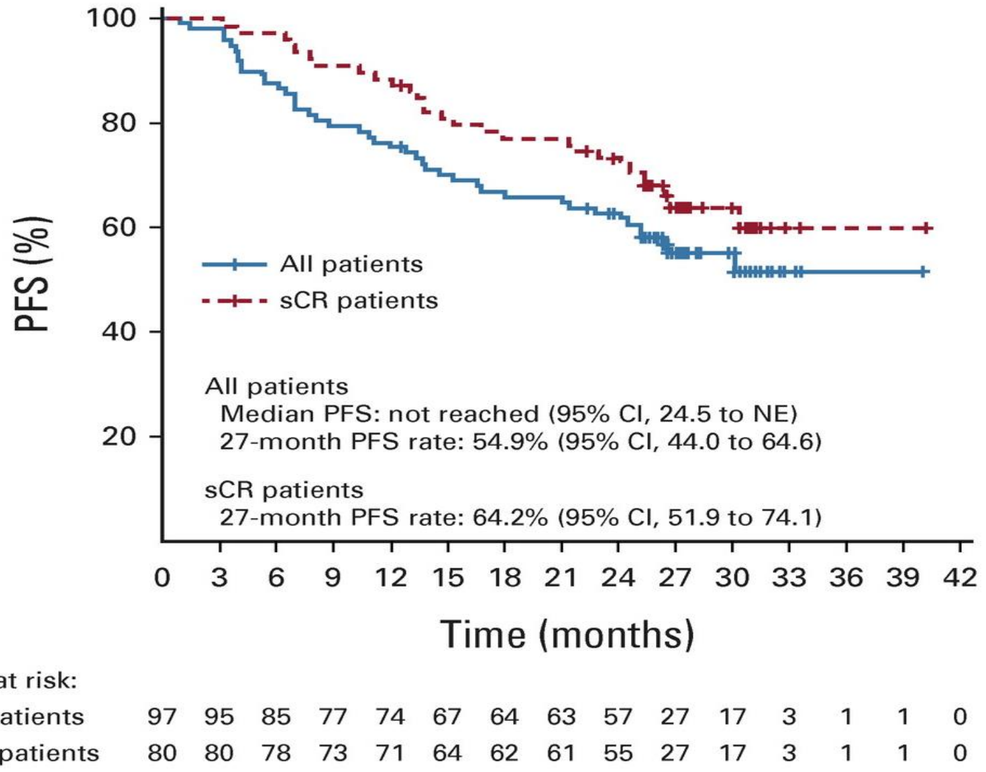


ORR 97.9% with 80.4% achieving sCR; response rates comparable across subgroups

Berdeja JG, *et al*. Lancet 2021
Usmani S, *et al*. ASCO 2022

CAR T cells are active against myeloma cells with clinical impact on survival in refractory/relapsed patients

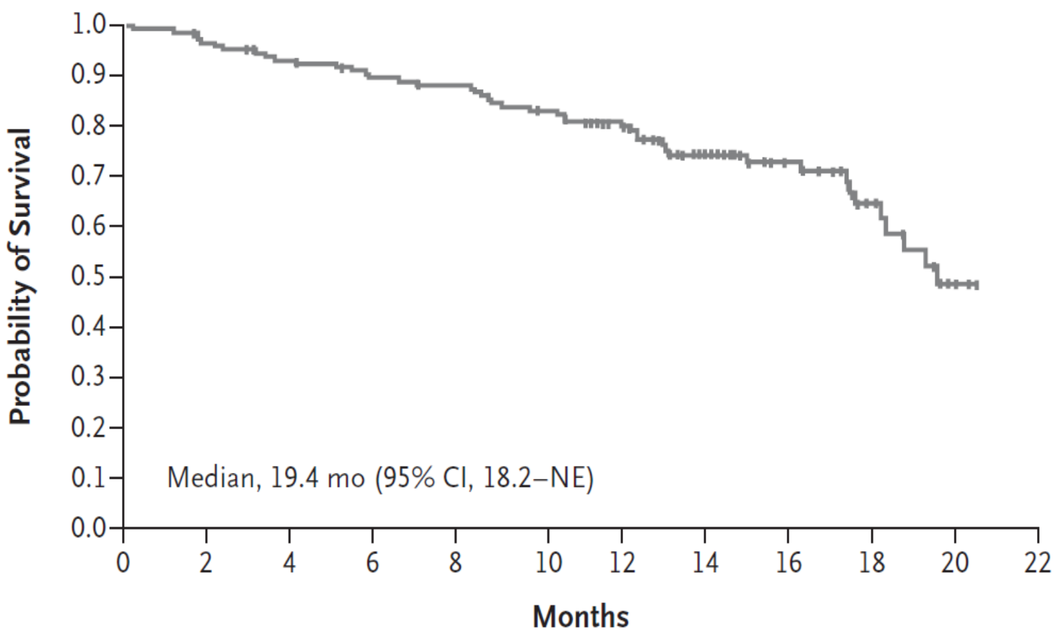


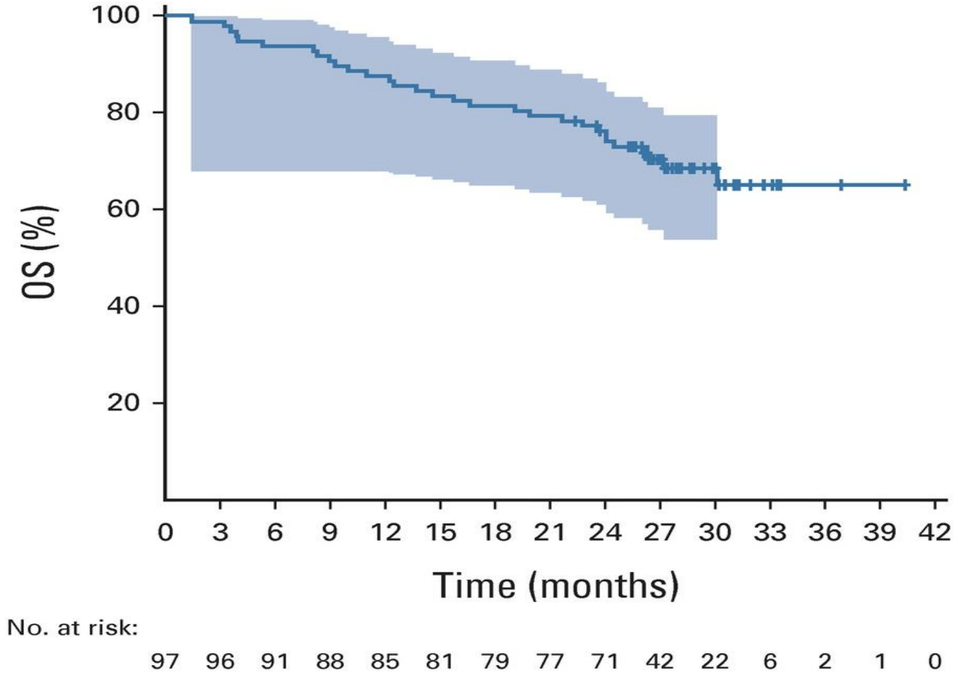


__CAR-T:__ chimeric antigen receptor T-cell; __CI:__ confidence Interval; __CR:__ complete response; __PR:__ partial response; __sCR:__ stringent complete response; __VGPR:__ very good partial response.

__1.__ Munshi NC, et al. N Engl J Med. 2021;384(8):705-716; __2.__ Martin, et al. JCO 2022

Overall survival - Ide-cel and Cilta-cel

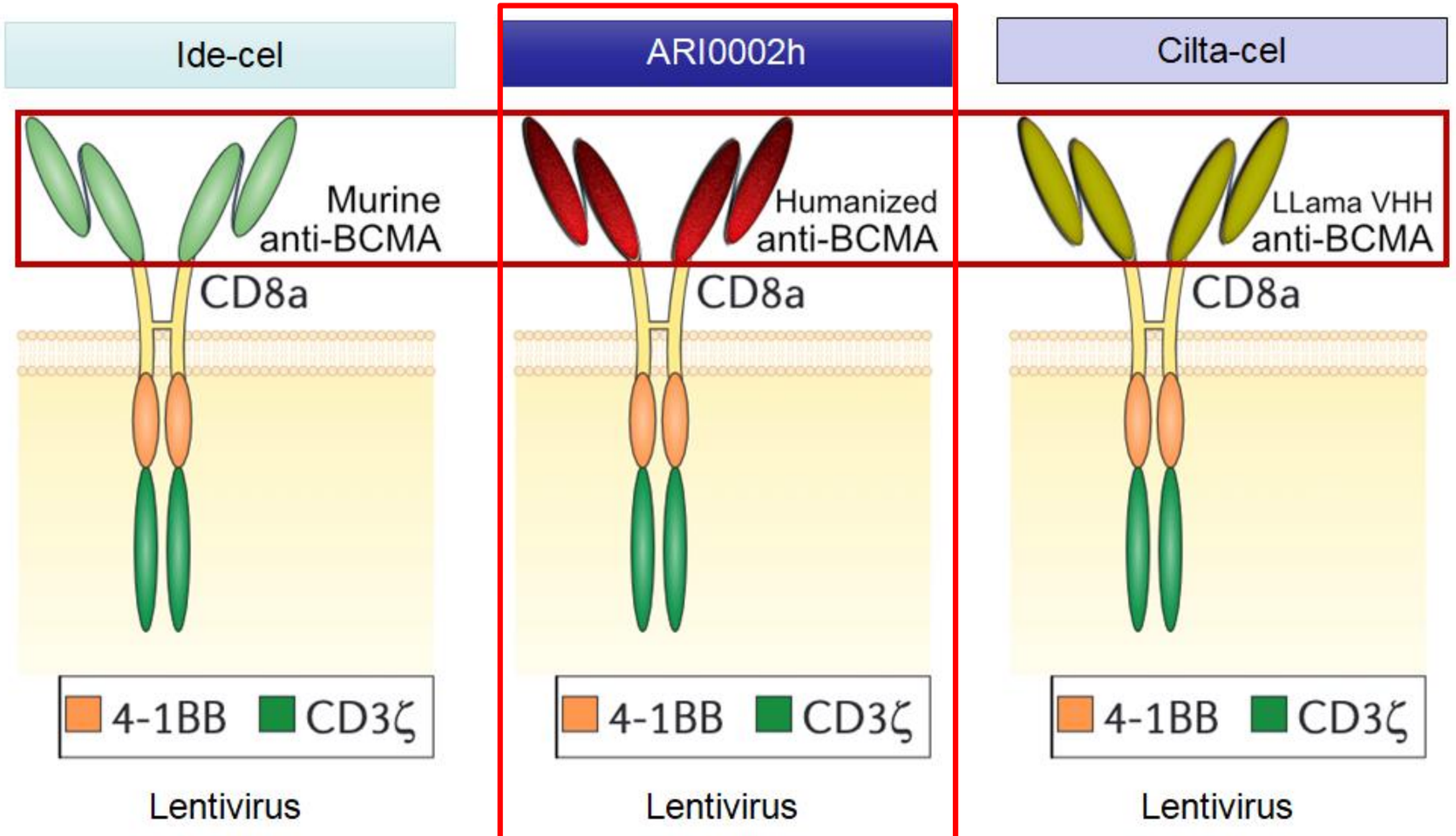




__CI:__ confidence Interval; __mo:__ months; __OS:__ overall survival; __sCR:__ stringent complete response.

__1.__ Munshi NC, et al. N Engl J Med. 2021;384(8):705-716; __2.__ Martin T, et al. JCO 2022.

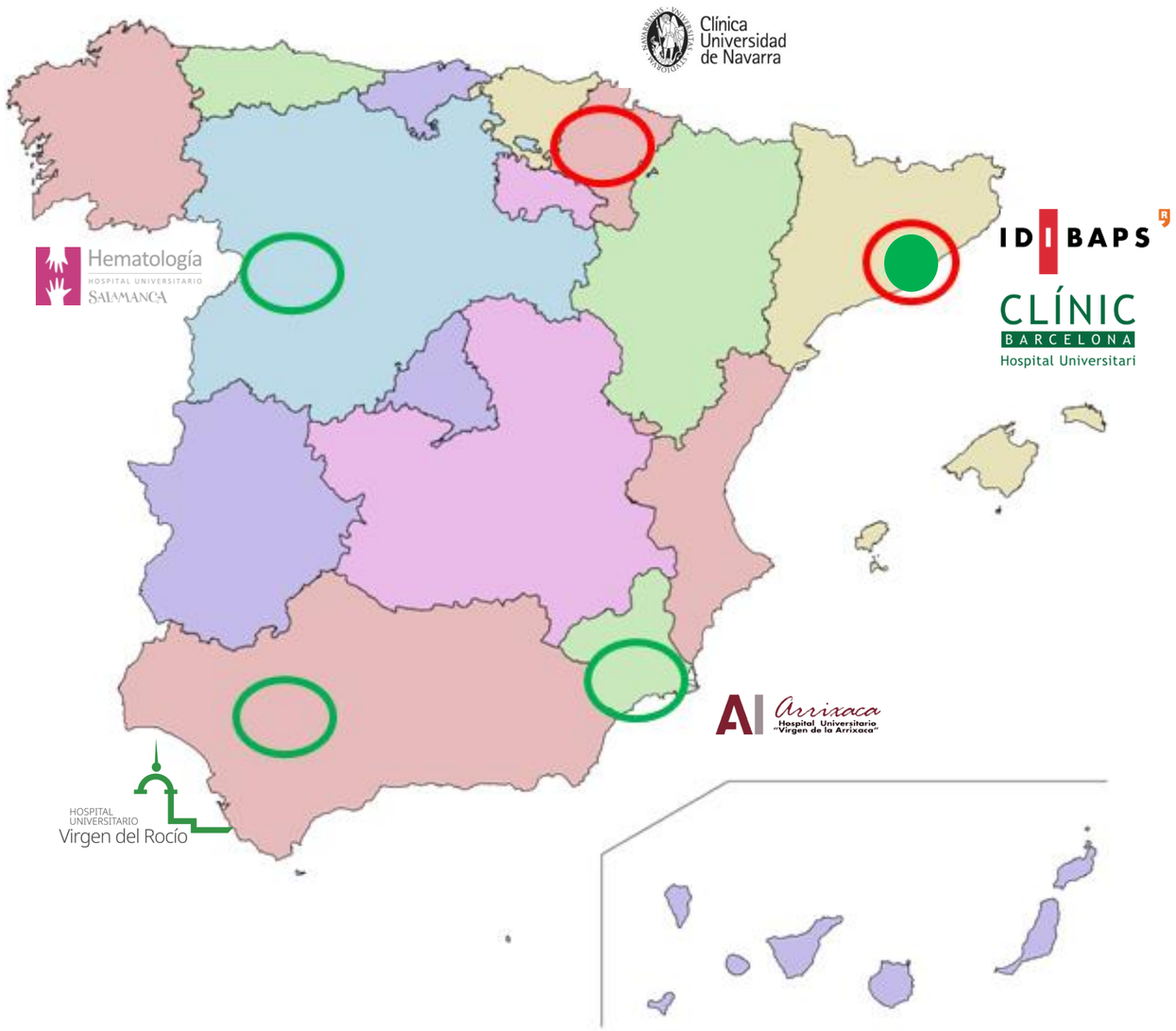
ARI0002h against BCMA in MM



Idecabtagene vicleucel

Ciltacabtagene autoleucel

CARTBCMA-HCB-01 Clinical Trial
(NCT 04309981)



Coordination:

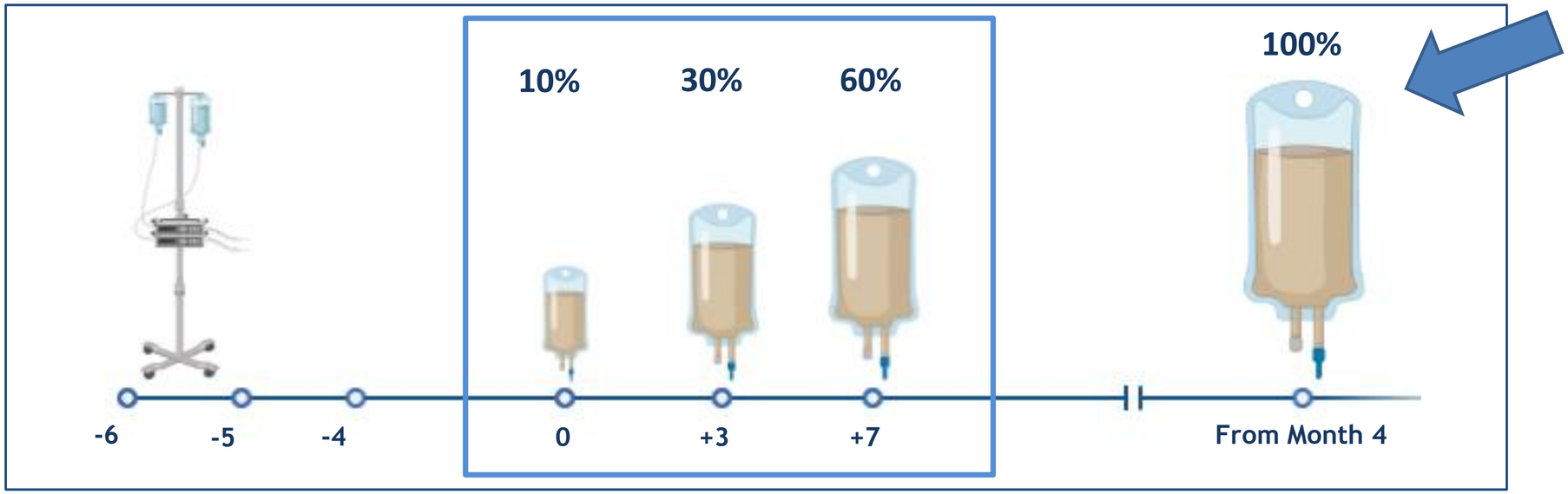
Hospital Clínic/IDIBAPS, **Barcelona**

Centers:

- Hospital Clínic, **Barcelona**
- Hospital Universitario de **Salamanca**
- Clínica Universidad de Navarra, **Pamplona**
- Hospital U. Virgen de la Arrixaca, **Murcia**
- Hospital Virgen del Rocío, **Sevilla**

Clinical trial main features

Lentivirally-transduced autologous T-cells
Fractionated infusion (10-30-60%)
Second dose after 4 months of the first infusion



Fludarabine 30 mg/m2/day
Cyclophosphamide 300 mg/m2/day
for 3 days

3x10^6 CART/kg
fractionated in 0.3/0.9/1.8

Up to 3x10^6 CART/kg
single dose

Oliver-Caldés *et al*. Lancet Oncol 2023

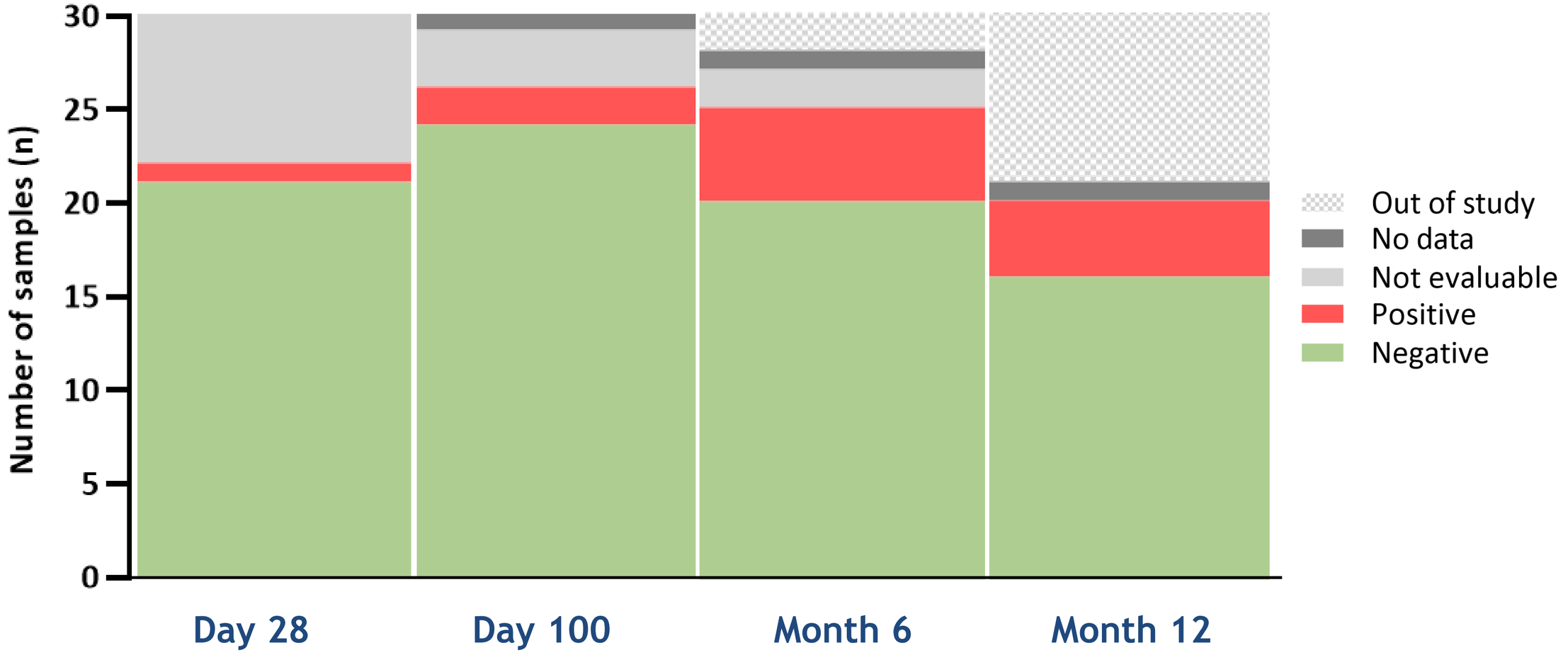
Efficacy: Response rate

Overall response rate in the first 3 months, n (%)	30 (100%)
Partial response, n (%)	6 (20%)
Very good partial response, n (%)	9 (30%)
Complete response, n (%)	15 (50%)
Median time to best response, days (95% CI)	99 (29-108)
Overall response rate, n (%)*	30 (100%)
Partial response, n (%)*	2 (7%)
Very good partial response, n (%)*	8 (27%)
Complete response, n (%)*	20 (67%)

Median follow-up 18 months (IQR 15-20)

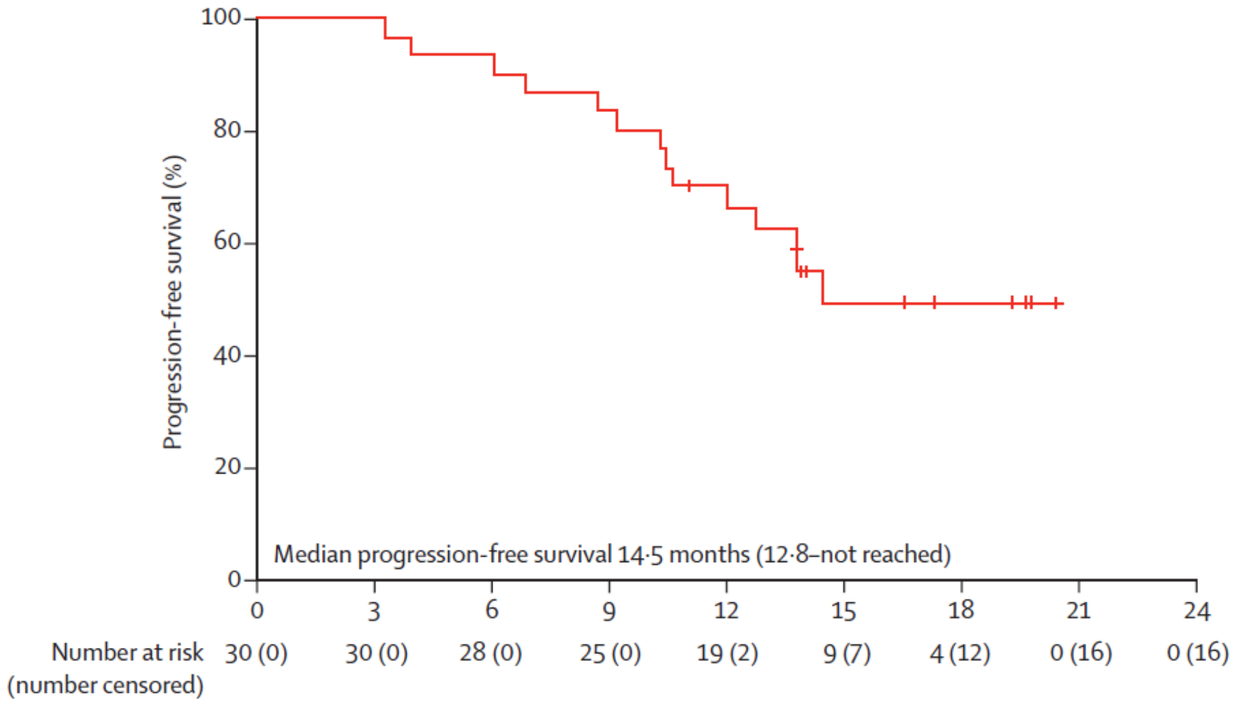
Oliver-Caldés *et al*. Lancet Oncol 2023

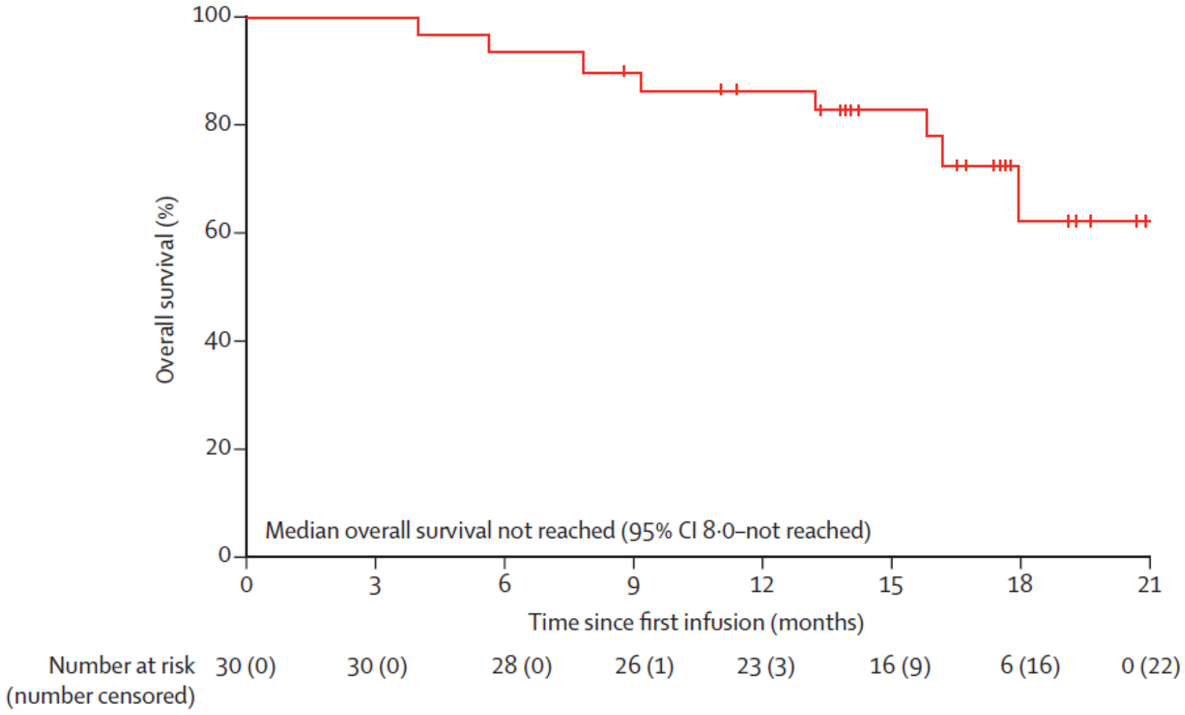
Minimal residual disease (MRD) by Next Generation Flow (NGF)



Oliver-Caldés *et al*. Lancet Oncol 2023

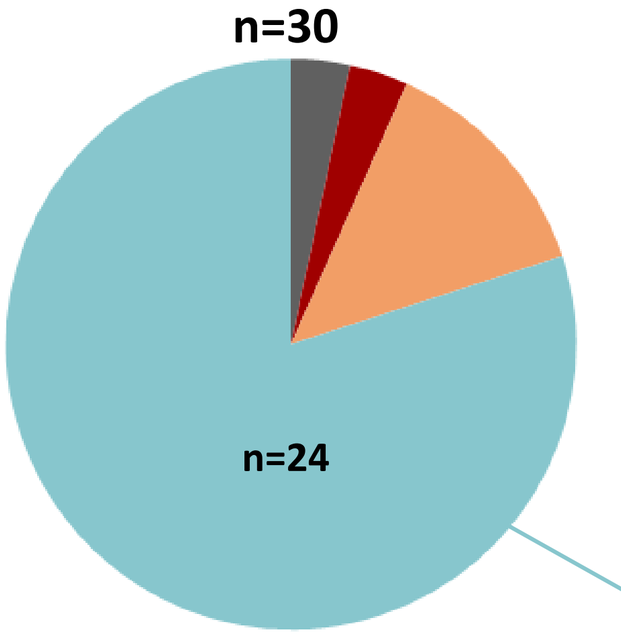
Efficacy: Progression-free survival and overall survival

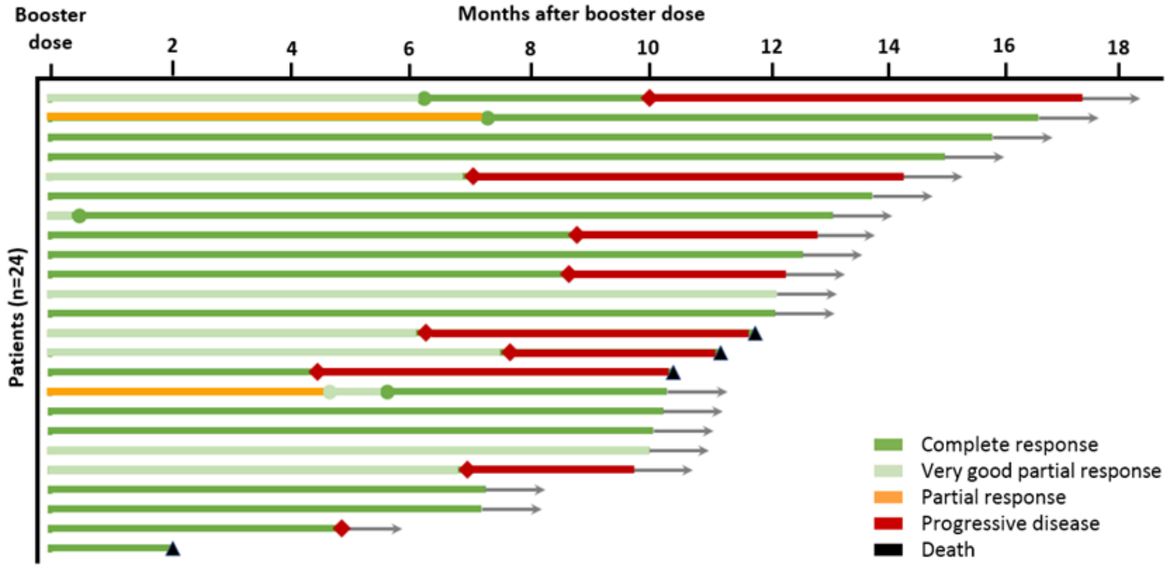


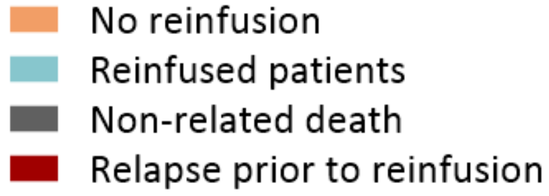


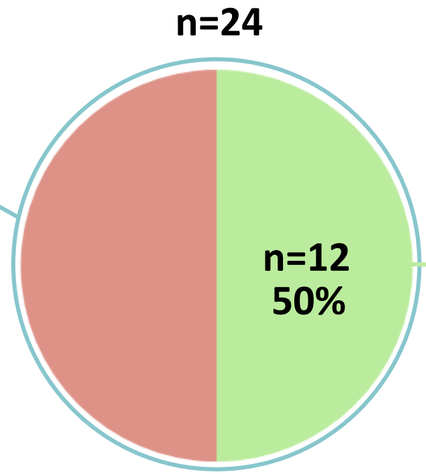
Oliver-Caldés *et al*. Lancet Oncol 2023

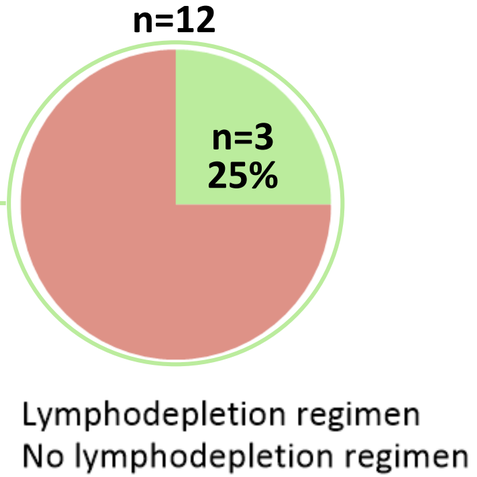
Efficacy: Second Infusion (booster)







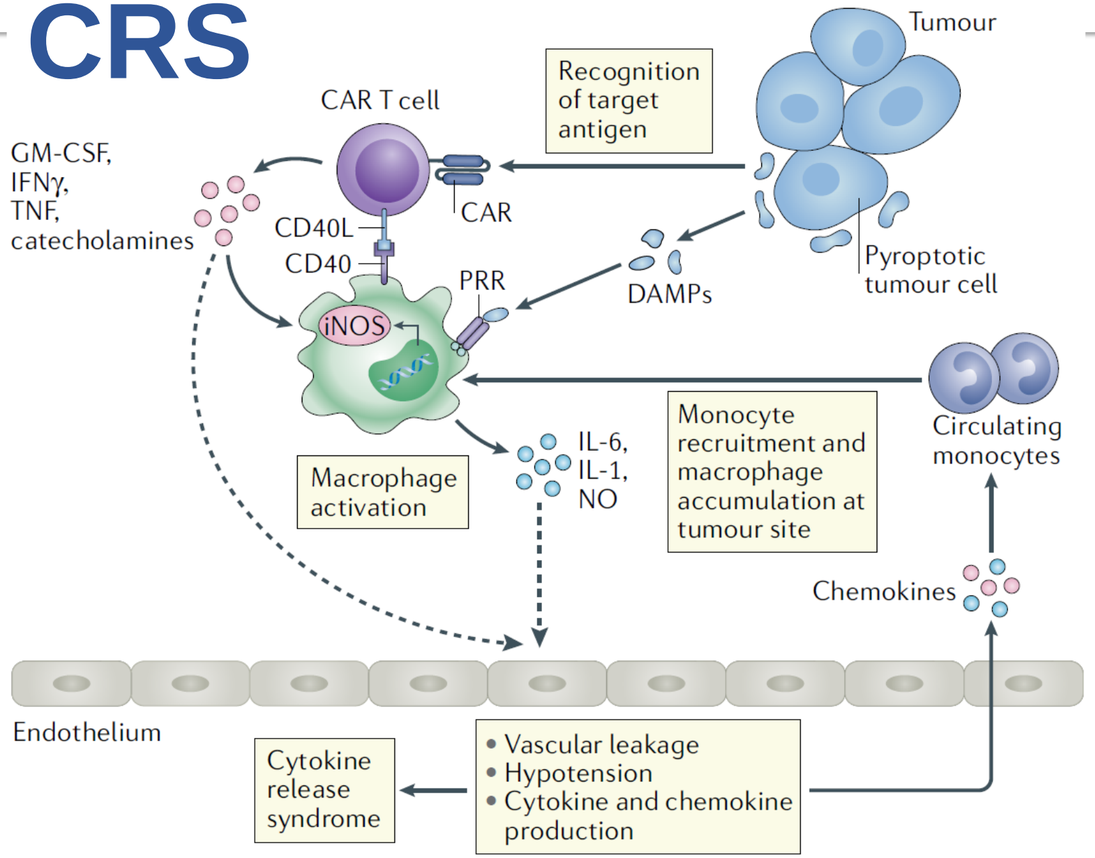


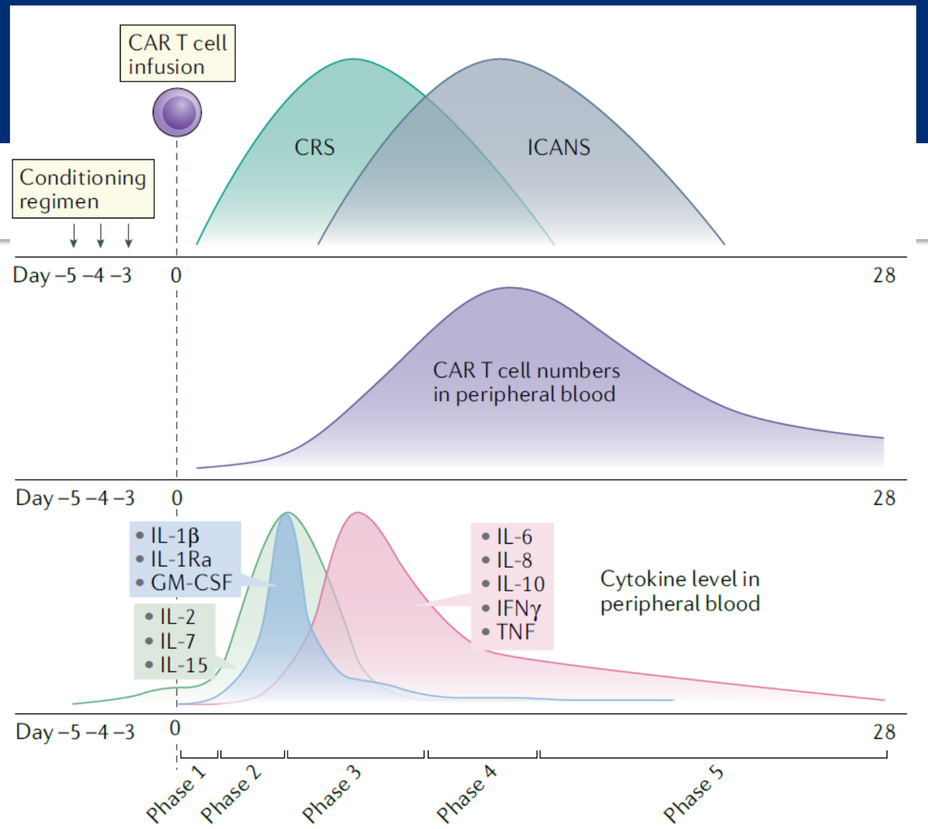


Oliver-Caldés *et al*. Lancet Oncol 2023

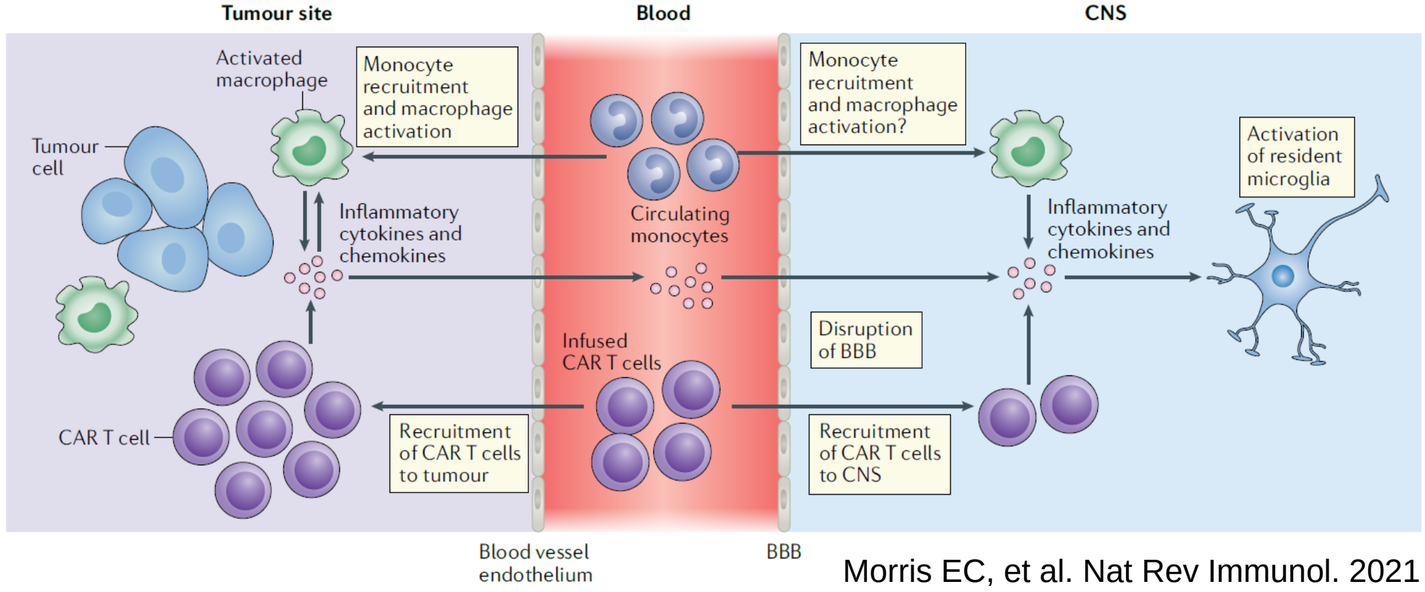
CAR Toxicity – CRS and ICANS

CRS





ICANS



Morris EC, et al. Nat Rev Immunol. 2021

CAR-T cell toxicity – CRS and ICANS

Síndrome de liberación de citocinas (CRS)		
Parámetro	**Ide-cel**	**Cilta-cel**
Cualquier evento (%) • Grado ≥ 3	84 6	95 5
Tiempo de aparición, mediana (días)	1	7
Duración, mediana (días)	5	4
Medidas de soporte • Tocilizumab (%) • Corticosteroides (%) • Anakinra (%)	 52 15 2	 69 22 19
Síndrome de neurotoxicidad asociada a células inmunoefectoras (ICANS)		
Parámetro	**Ide-cel**	**Cilta-cel**
Evento número (%) • Grado ≥ 3	18 3	17 2
Tiempo de aparición, mediana (días)	2	8
Duración, mediana (días)	3	4
Medidas de soporte • Corticosteroides (%) • Tocilizumab (%) • Anakinra (%)	 8 2 < 1	 9 4 3

__CAR-T:__ chimeric antigen receptor T-cell; __CRS:__ cytokine release syndrome; __ICANS:__ immune-effector cell associated neurotoxicity syndrome.

__1.__ Munshi NC, et al. N Engl J Med. 2021;384(8):705-716; __2.__ Berdeja JG, et al. Lancet. 2021;398(10297):314-324.

Safety: Cytokine-release syndrome (CRS) and neurotoxicity

Adverse events of special interest	%	Grades
CRS	**63%**	Grade 1
	38%	Grade 2
ICANS	**0%**	-
Infusion reaction	3.3%	Grade 1
Tumour lysis syndrome	3.3%	Grade 2
Persistent cytopenias	67%	

CRS: cytokine release syndrome;
ICANS: Immune effector cell-associated neurotoxicity syndrome.

Median onset of CRS: 7 days (range 5-8)

Median duration of CRS: 2 days (range 1-14)

Use of Tocilizumab: 63%*

Use of corticosteroids: 10%

*mainly for persistent grade 1 CRS

Other relevant adverse events:

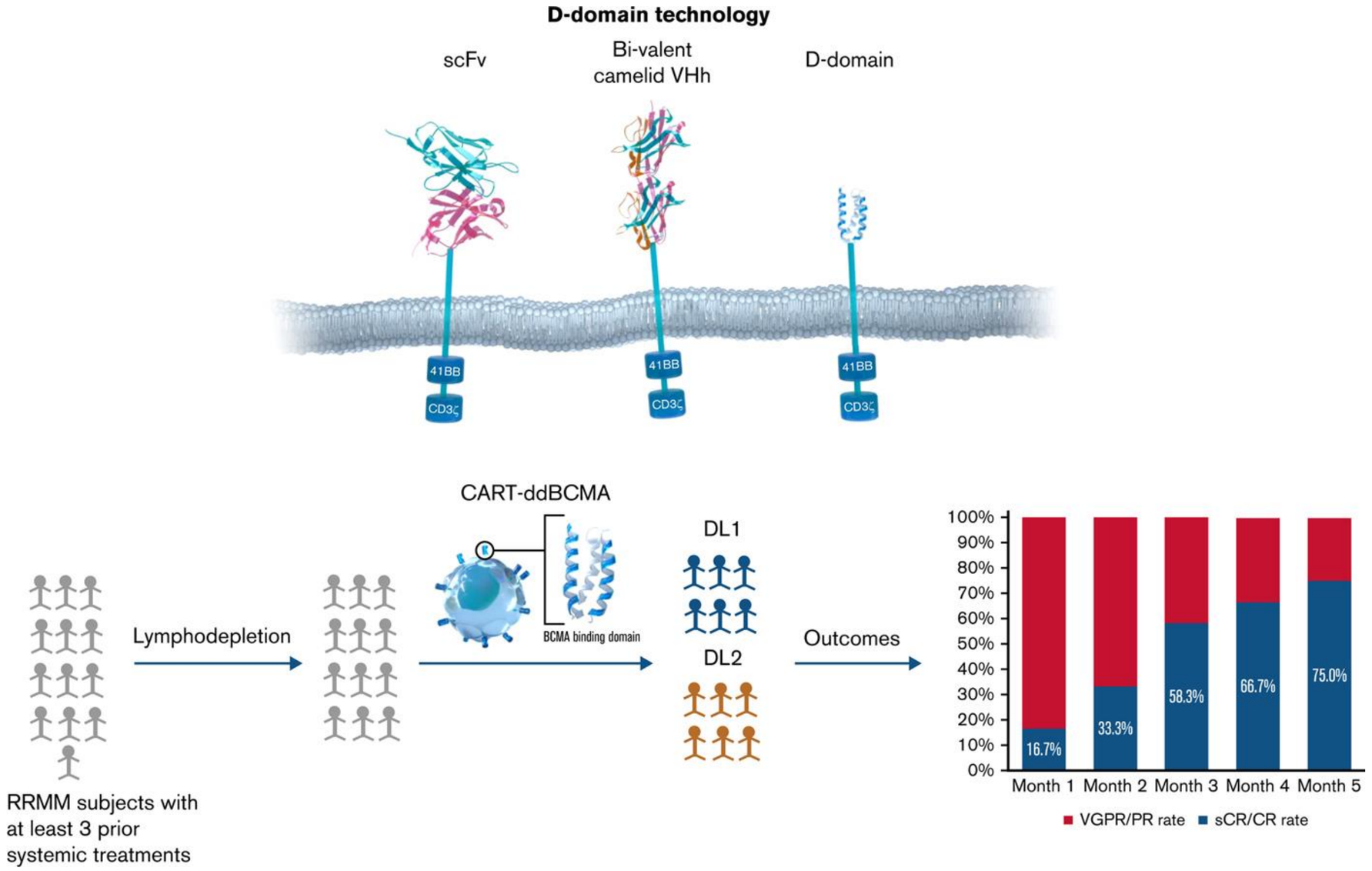
macrophage-activation syndrome (3),

hepatitis B reactivation (1), colon cancer (1; unrelated)

Infections: 67% of patients (23% grade ≥ 3)

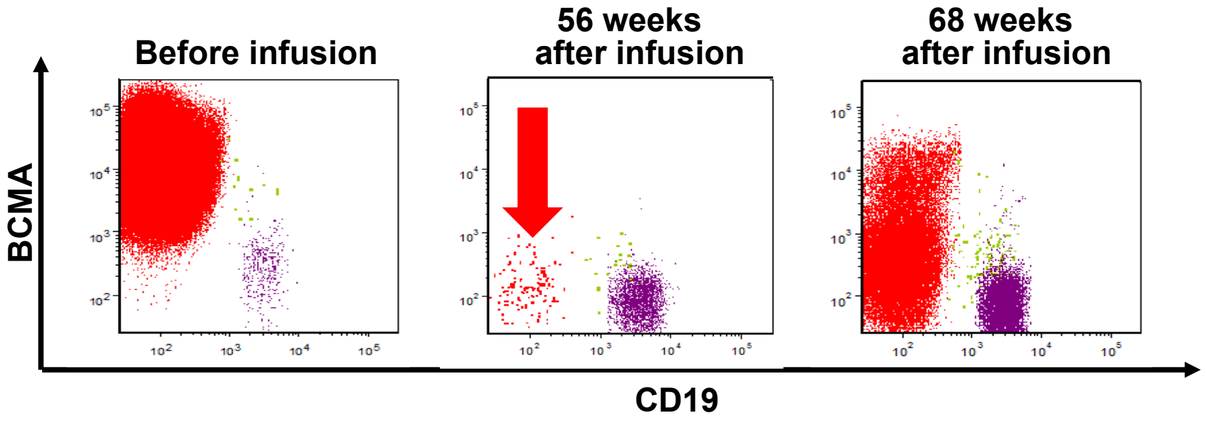
Oliver-Caldés *et al*. Lancet Oncol 2023

CAR-T-ddBCMA



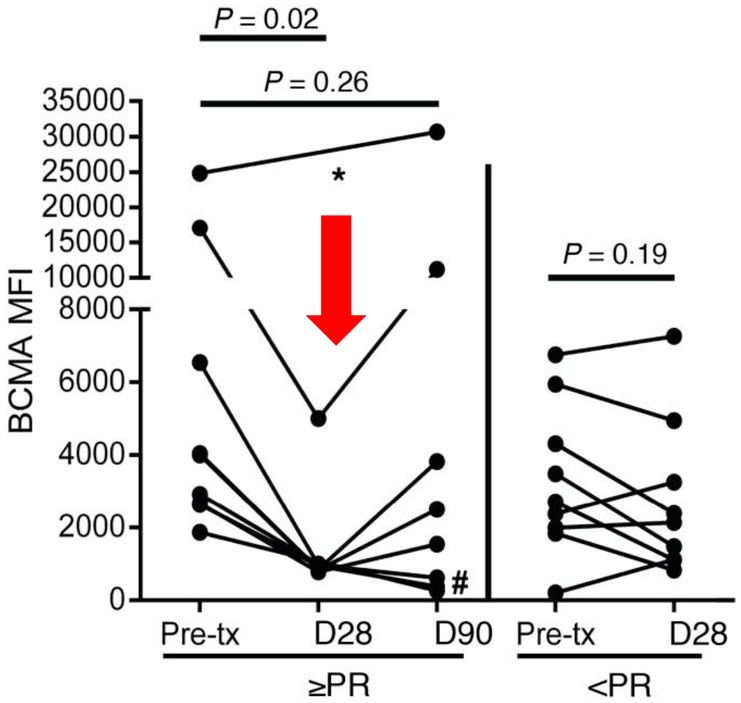
Frigault MJ, *et al*. Blood Adv 2023

Antigen escape / downregulation may be a significant clinical challenge in BCMA-CAR T-cell therapy



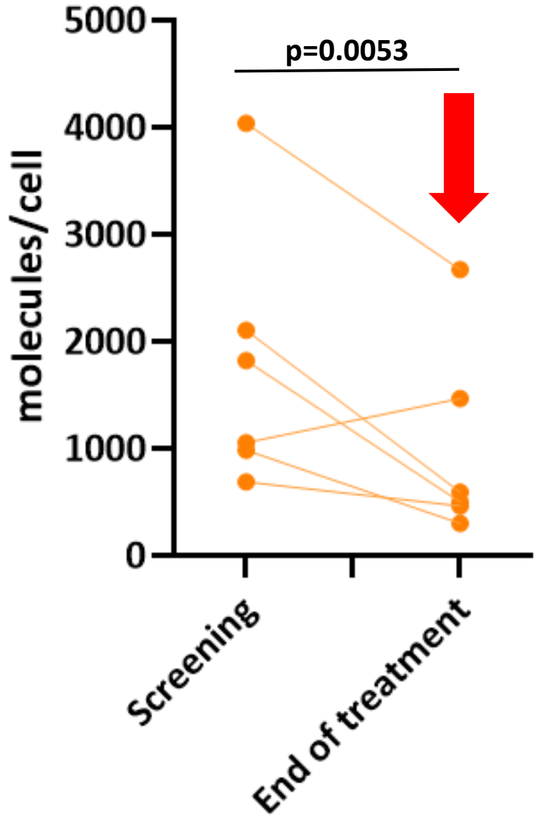
Red=myeloma plasma cells
Green=normal plasma cells
Purple=B cells

Brudno *et al*. JCO 2018



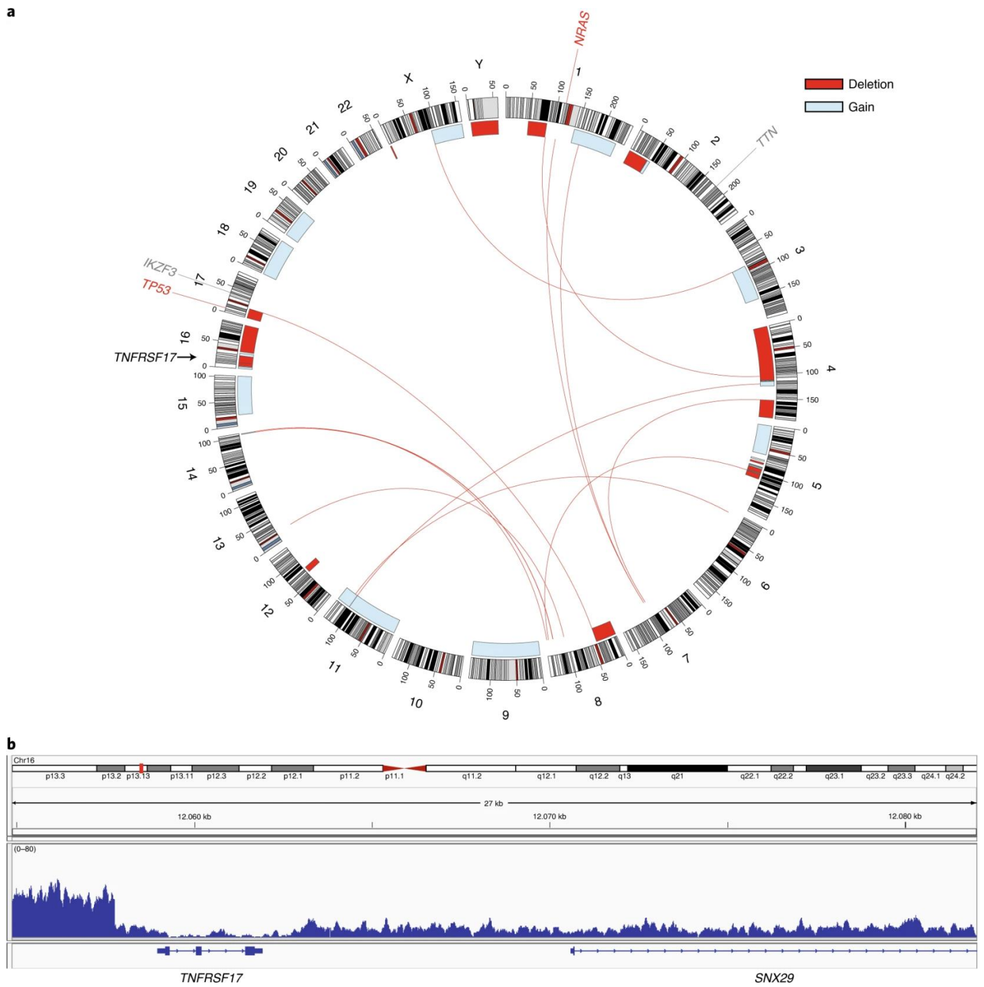
Cohen *et al*. JCI 2019

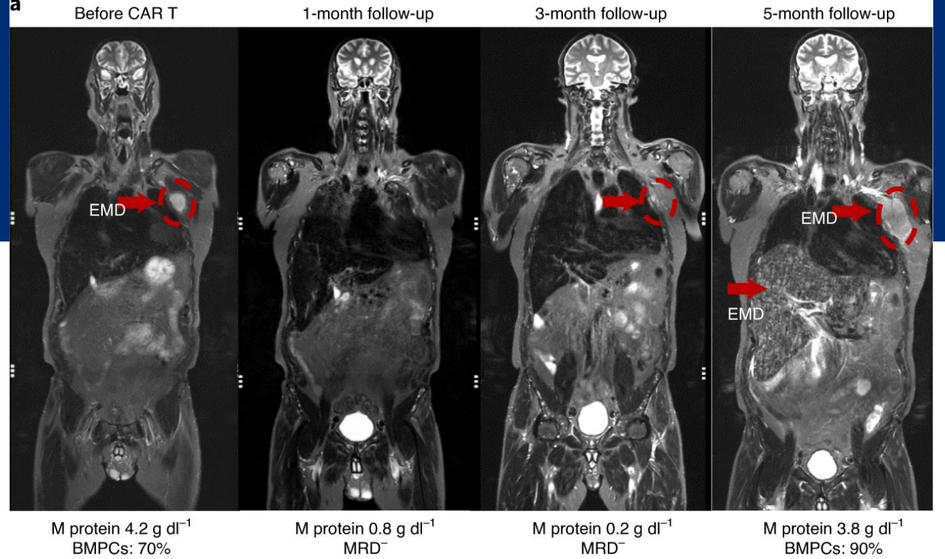
BCMA expression in bone marrow (BM) plasma cells (PC) of relapsed patients

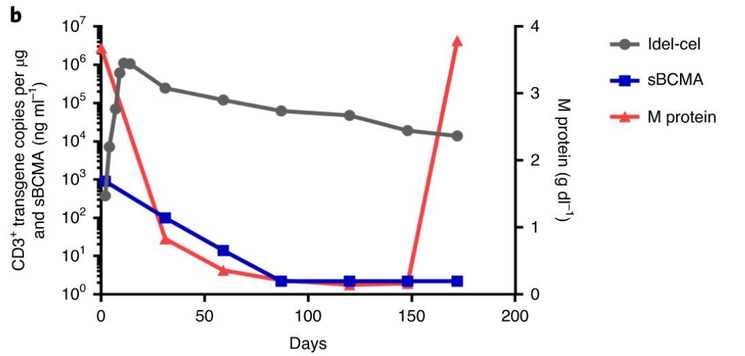


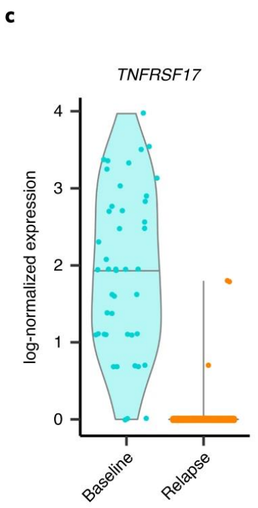
Oliver-Caldés *et al*. Lancet Oncol 2023

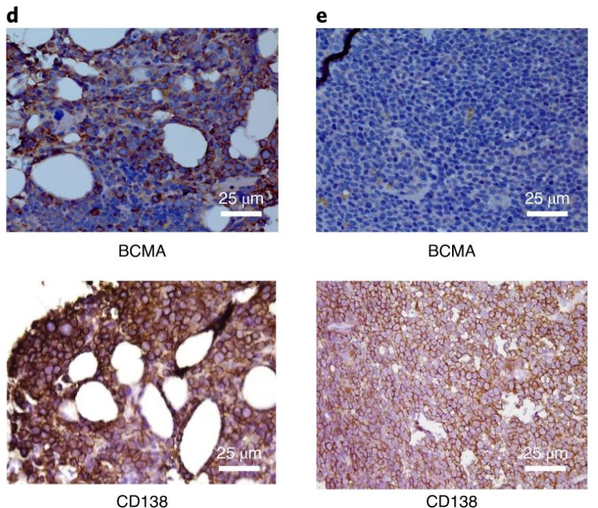
Homozygous BCMA gene deletion in response to anti-BCMA CAR T cells











Da Vià *et al*. Nat Med 2021

G Protein-Coupled Receptor Class C Group 5 Member D (GPRC5D)

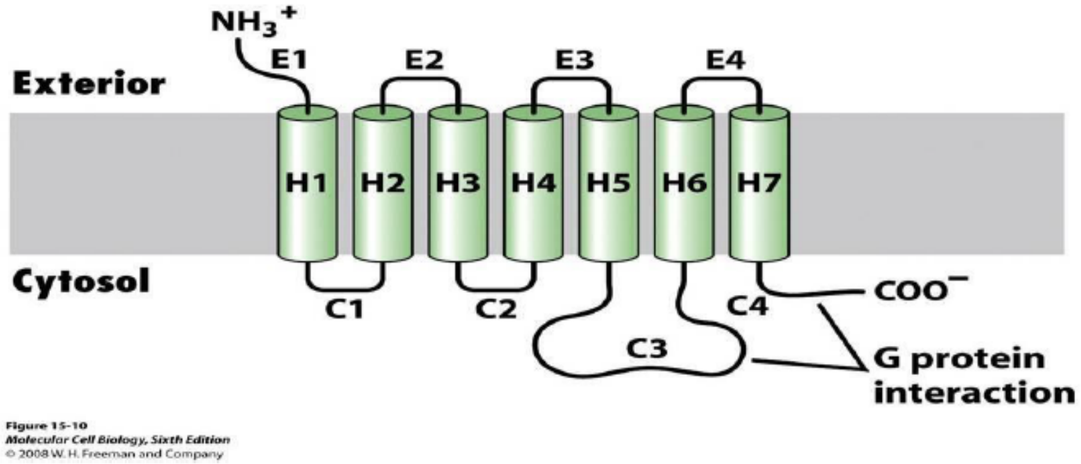
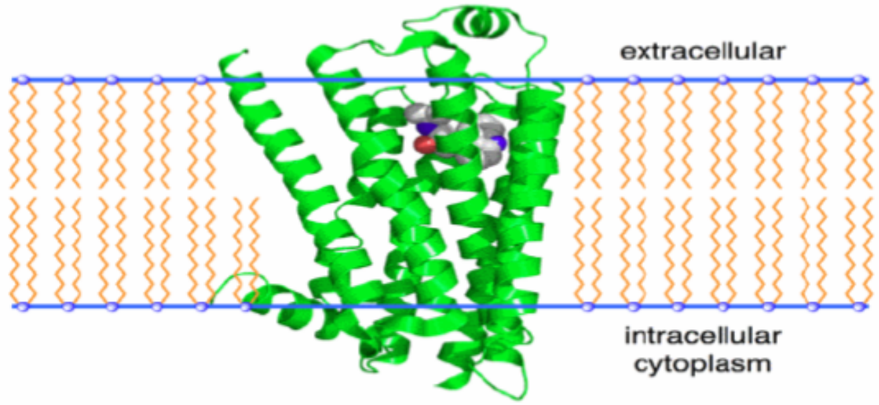


Figure 15-10
Molecular Cell Biology, Sixth Edition
© 2008 W. H. Freeman and Company



- Orphan 7 trans-membrane receptor
- mRNA overexpressed in MM marrow aspirates
- Expressed in hair follicle cells, a potentially immune privileged site

Smith *et al*, ASH 2018 and Sci Transl Med 2019

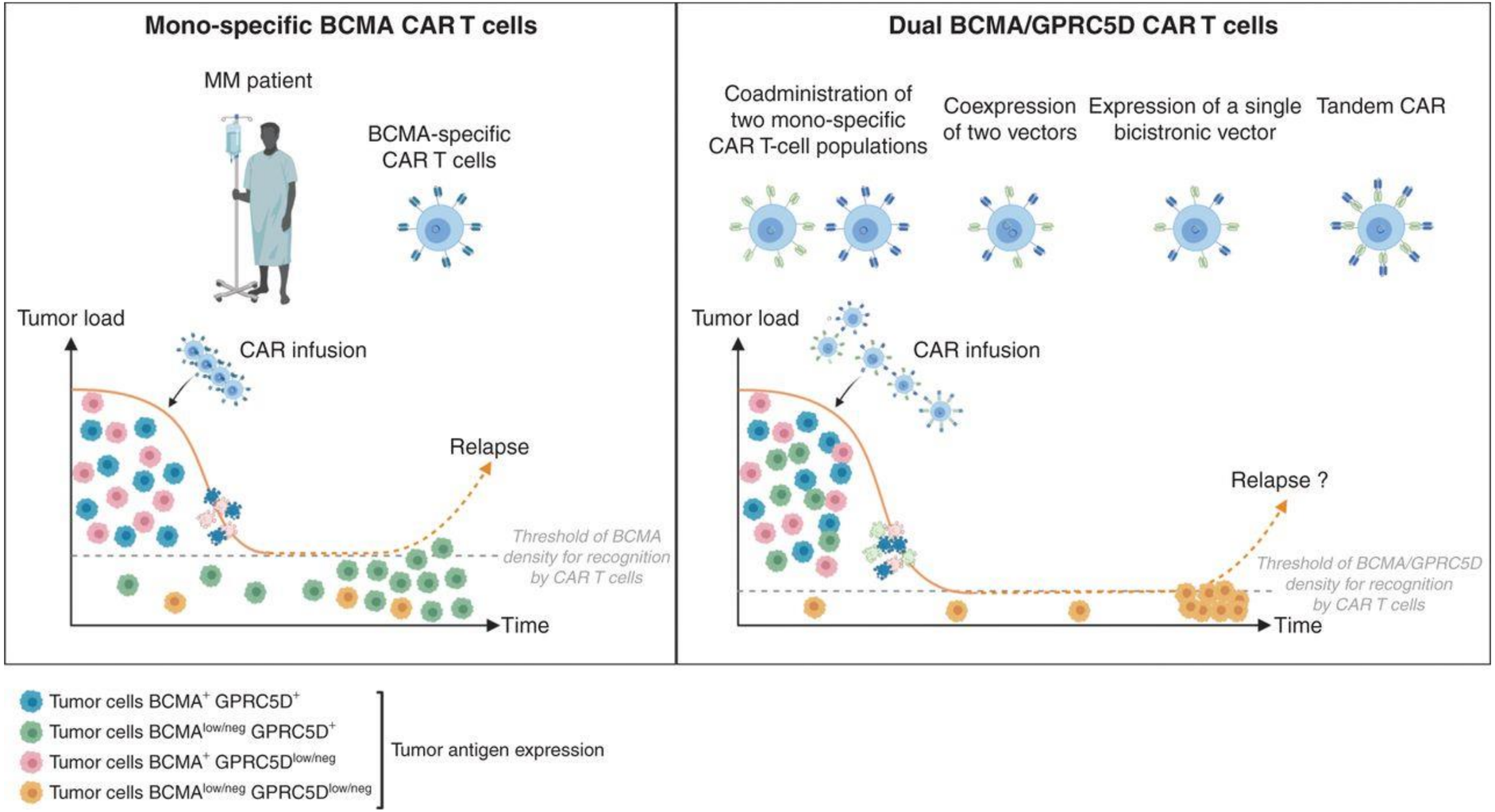
GPRC5D CAR-T: Clinical responses (n=17)

Response	All Patients		Previous BCMA Therapies		No Previous BCMA Therapies	
	All Dose Levels (N=17)	25×10^6–150×10^6 CAR T Cells (N=12)	All Dose Levels (N=10)	25×10^6–150×10^6 CAR T Cells (N=6)	All Dose Levels (N=7)	25×10^6–150×10^6 CAR T Cells (N=6)
	number (percent)					
Partial response or better	12 (71)	7 (58)	7 (70)	3 (50)	5 (71)	4 (67)
Very good partial response or better	10 (59)	5 (42)	6 (60)	2 (33)	4 (57)	3 (50)
Complete response or better	6 (35)	3 (25)	4 (40)	2 (33)	2 (29)	1 (17)
Negativity for MRD in bone marrow*	8 (47)	6 (50)	3 (30)	2 (33)	5 (71)	4 (67)

* Negativity for minimal residual disease (MRD) in bone marrow was assessed by means of 10-color flow cytometry with a sensitivity of 1 in 10^5 at 4 weeks after CAR T-cell therapy, at the occurrence of a complete response, and as clinically indicated.

Mailankody S *et al*. NEJM 2022

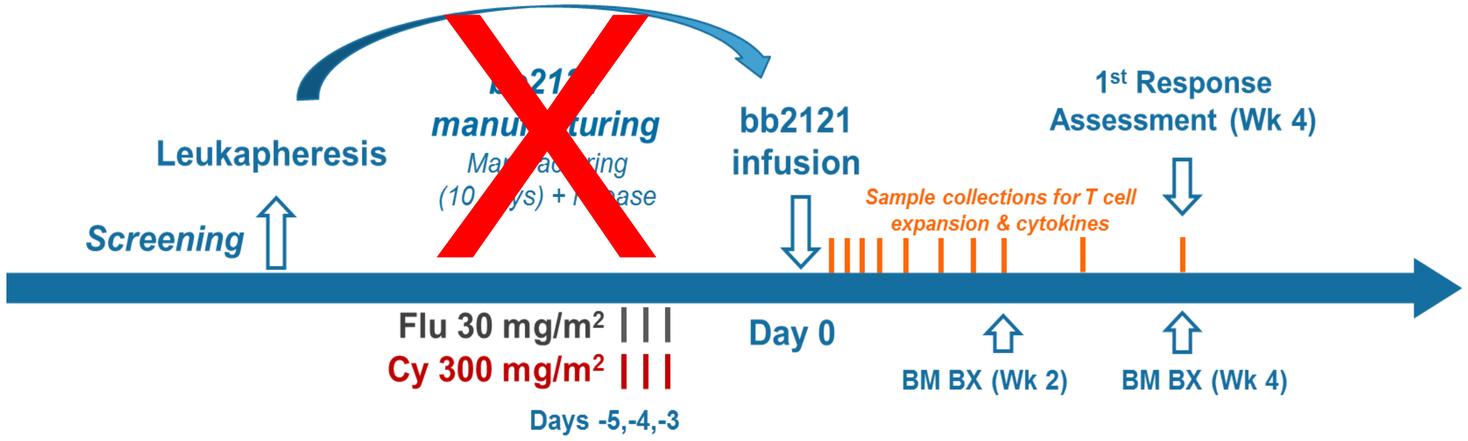
Dual-targeting model for MM (BCMA and GPRC5D)



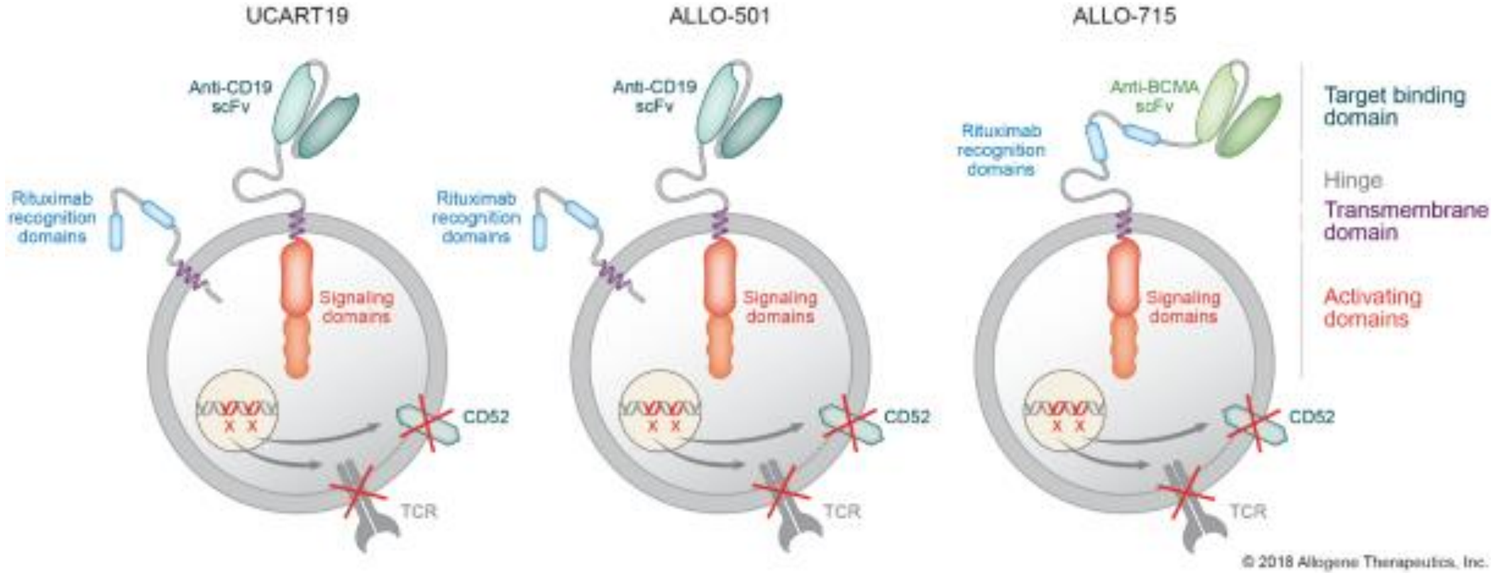
__BCMA__: B cell maturation antigen; __CAR-T__: chimeric antigen receptor T-cell; __GPRC5D__: G protein-coupled receptor class C group 5 member D; __MM__: multiple myeloma

__1__. Simon S, Riddell SR. Blood Cancer Discov. 2020;1(2):130-133; __2__. Fernández de Larrea C, et al. Blood Cancer Discov. 2020;1(2):146-154.

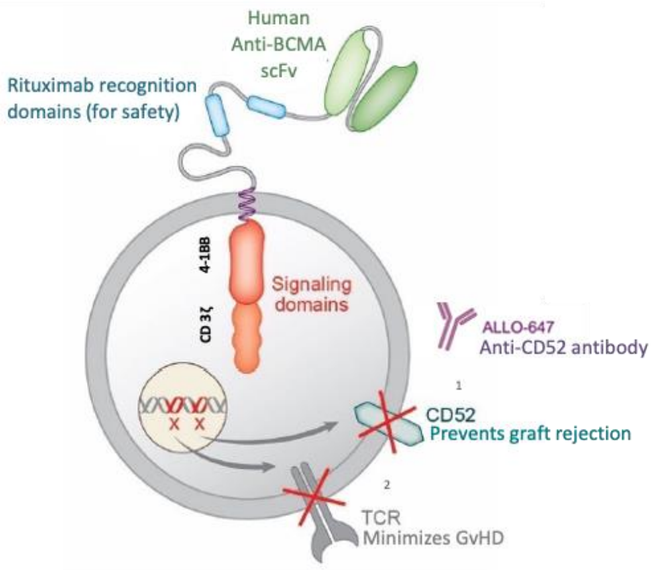
Improving the access: Allogeneic CAR-T cells

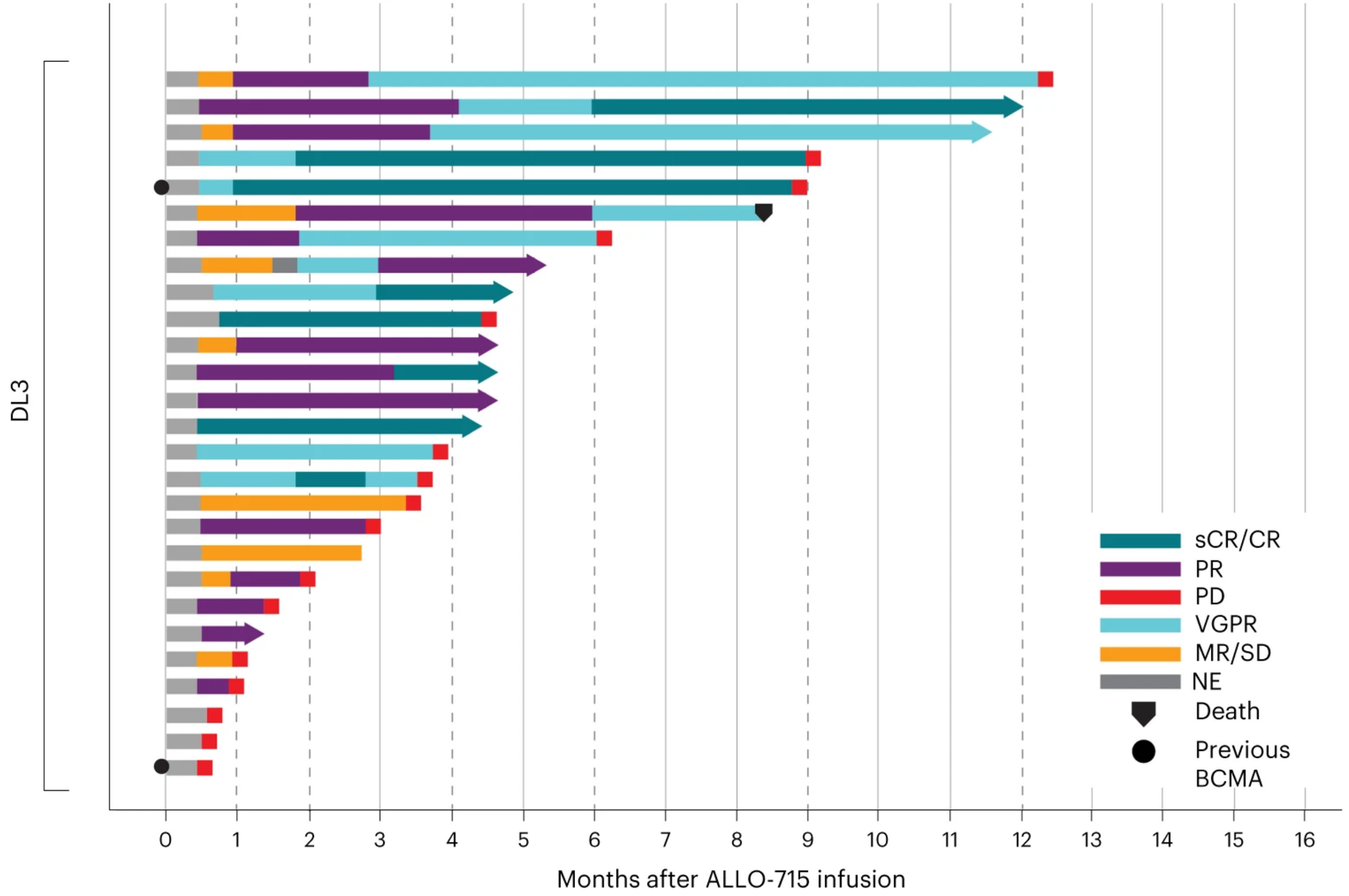


- *"Off the shelf"*
- Healthier T-cells
- Better time vein-to-vein



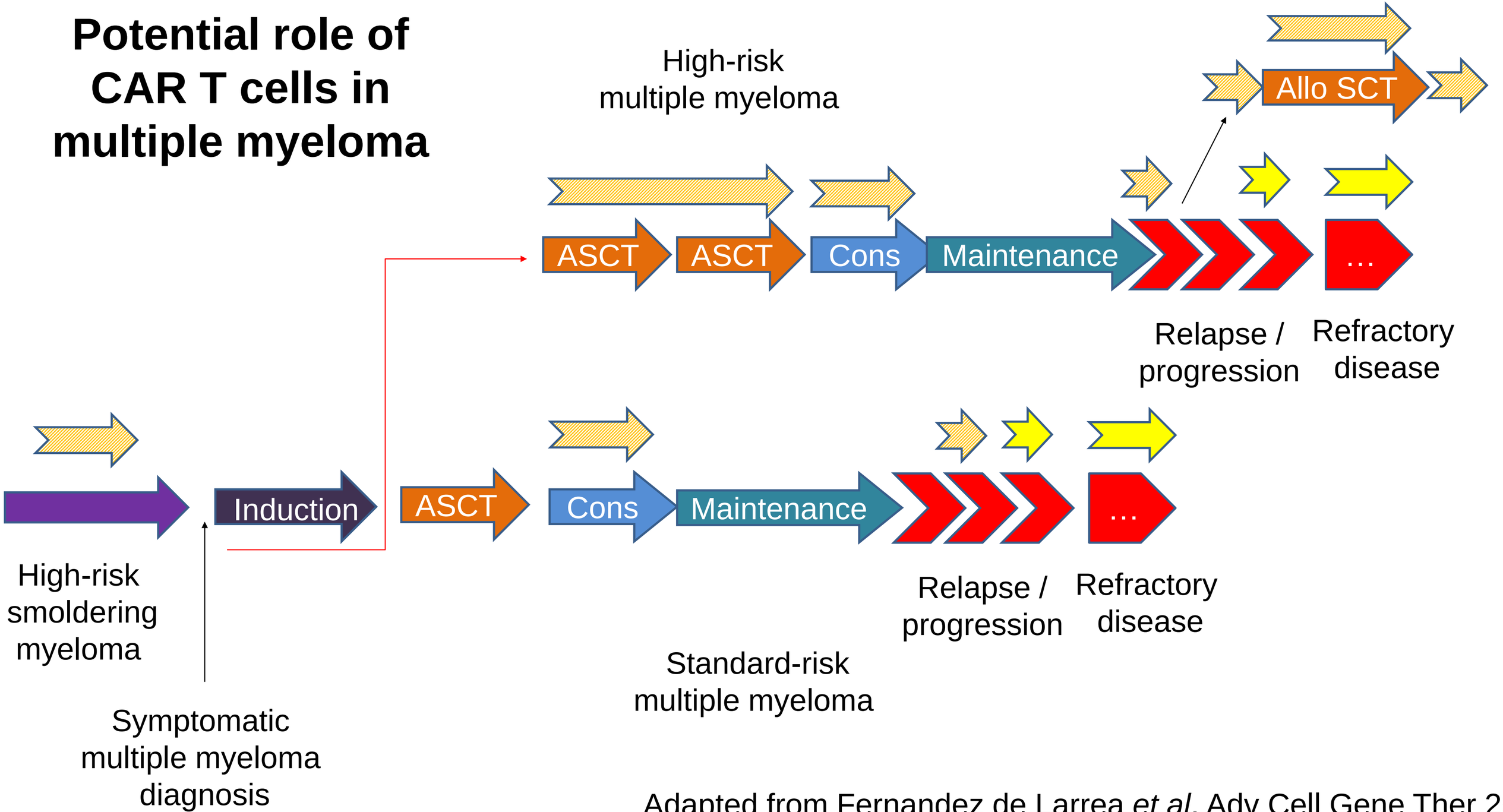
ALLO-715 : First Allogeneic anti-BCMA CAR-T





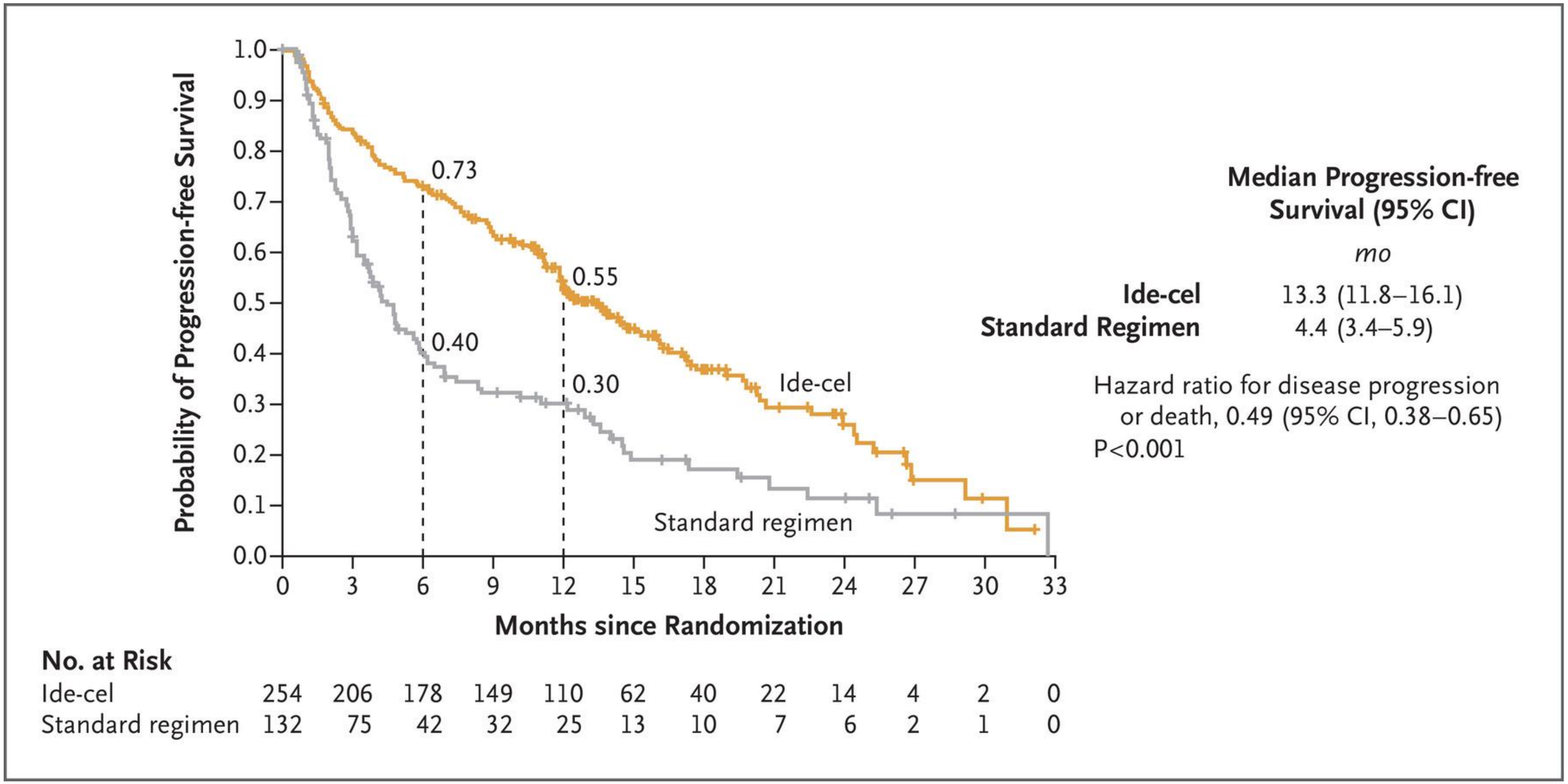
Mailankody *et al.* Nat Medicine 2023

Potential role of CAR T cells in multiple myeloma



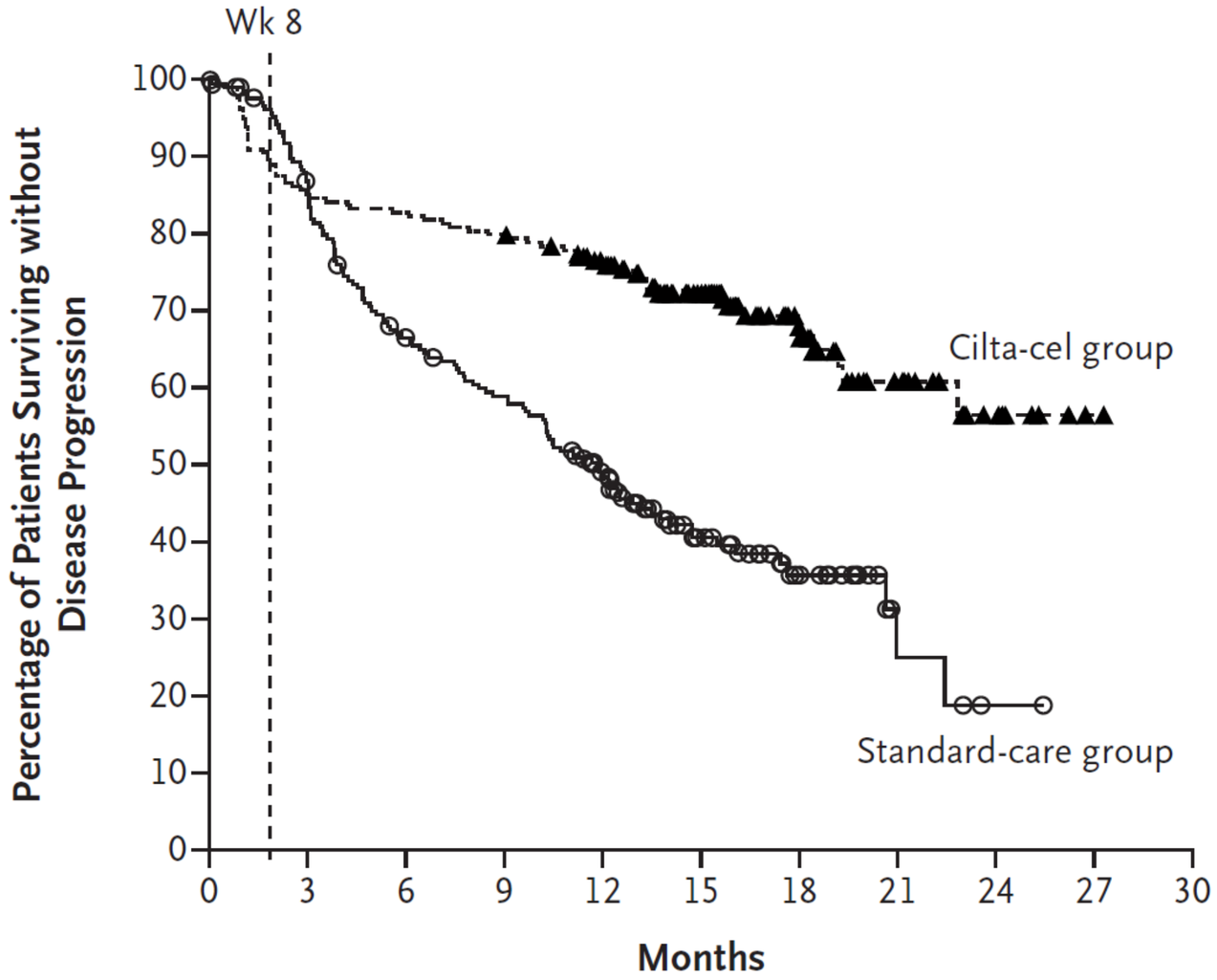
Adapted from Fernandez de Larrea *et al*. Adv Cell Gene Ther 201

Ide-cel or Standard Regimens in Refractory MM



Rodríguez-Otero *et al.* NEJM 2023

Cilta-cel or Standard Regimens in Refractory MM



San Miguel *et al.* NEJM 2023

Randomized Phase 3 study in Newly Diagnosed, Transplant Eligible Patients vs ASCT

CARTITUDE-6

EMN28

Key eligibility criteria:

- Newly diagnosed Patients
  - Age=< 70
  - Eligible for initial ASCT
- **Sample Size: ~750**

1:1 Randomization

scDara + VRd (x4) then ASCT, then D-VRd consolidation (x2), then D+R maintenance* (until PD)

D+VRd 6 cycles → **Cilta-cel** → **D+R (max 2 yrs)** → **Obse rvatio n**

Follow-up until PD → **Long-term follow-up for survival, subseq. therapie s & SPMs**

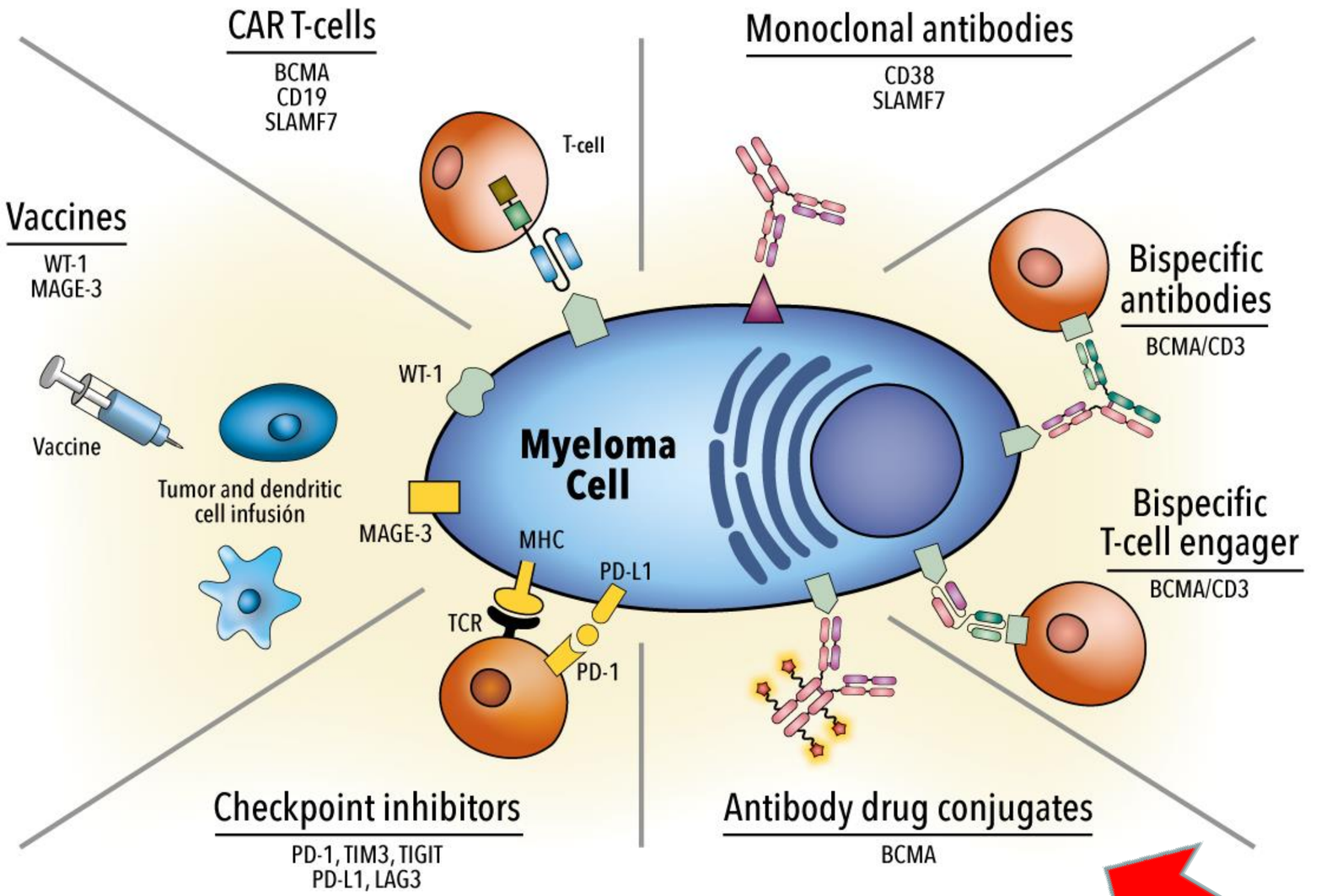
Assessment of PFS

Stratification factors:

a) **ISS staging**
b) **Cytogenetics**
c) **Age**

***based on DARA-MMY3014 registration study.** Includes DARA-stopping rules after 2 years for MRD-negativity.

Primary endpoint:
Sustained MRD neg CR
Key Secondary endpoint: PFS

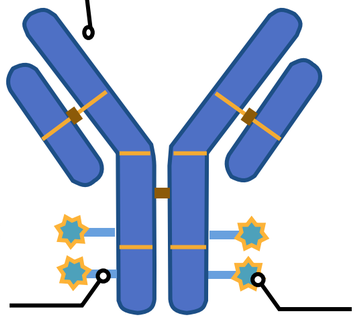


Rodriguez-Lobato *et al*. Hemato 2020

Belantamab mafodotin - Overview

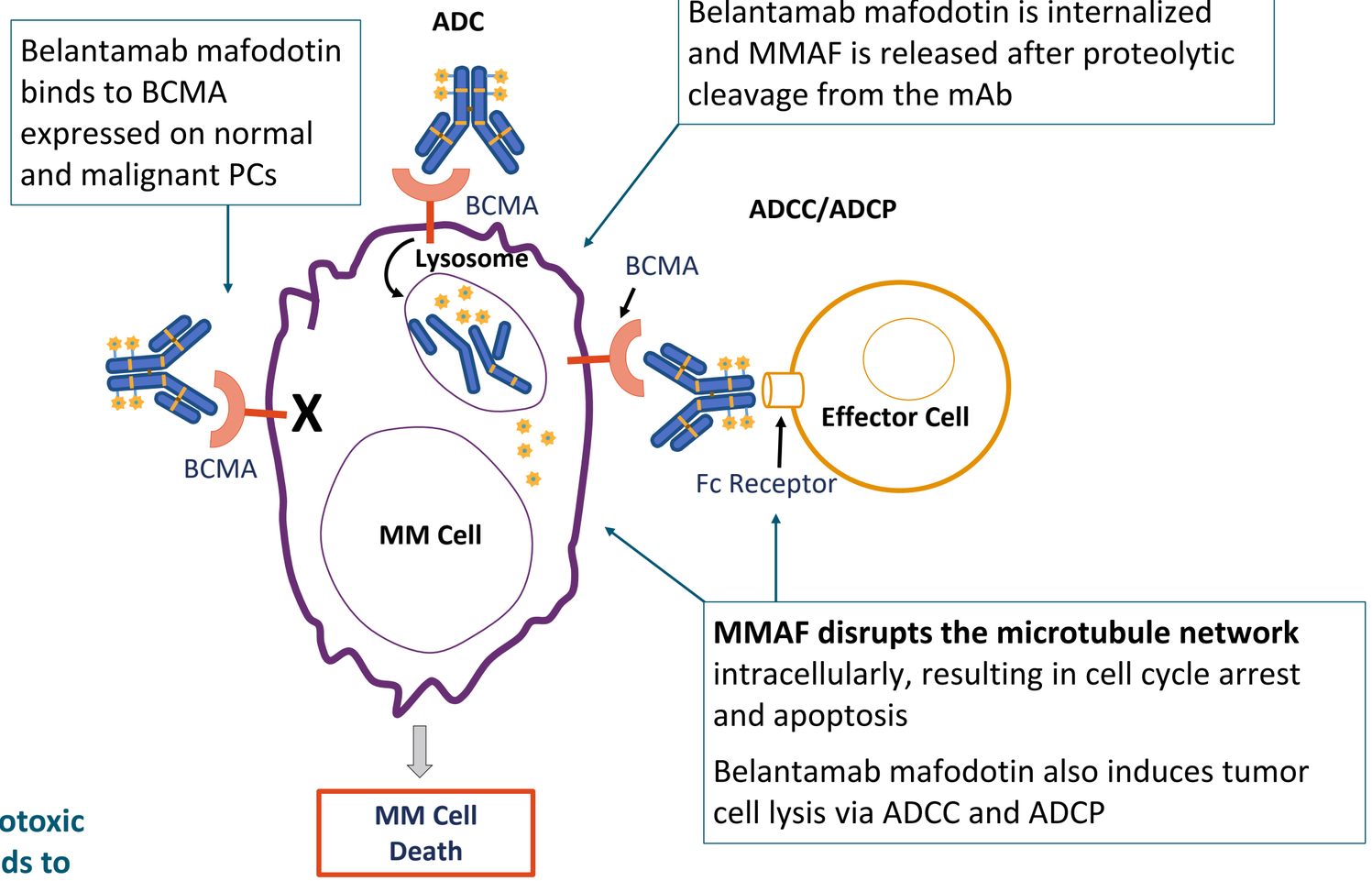
- **Belantamab mafodotin**: a BCMA-directed antibody and microtubule inhibitor conjugate comprising 3 components

1 **Humanized anti-BCMA IgG1 mAb that binds to BCMA-expressing MM cells**



Protease-resistant maleimidocaproyl linker that joins MMAF to mAb and releases payload only in target cell 3

2 **MMAF: microtubule-disrupting cytotoxic agent that leads to apoptosis of BCMA-expressing MM cells**

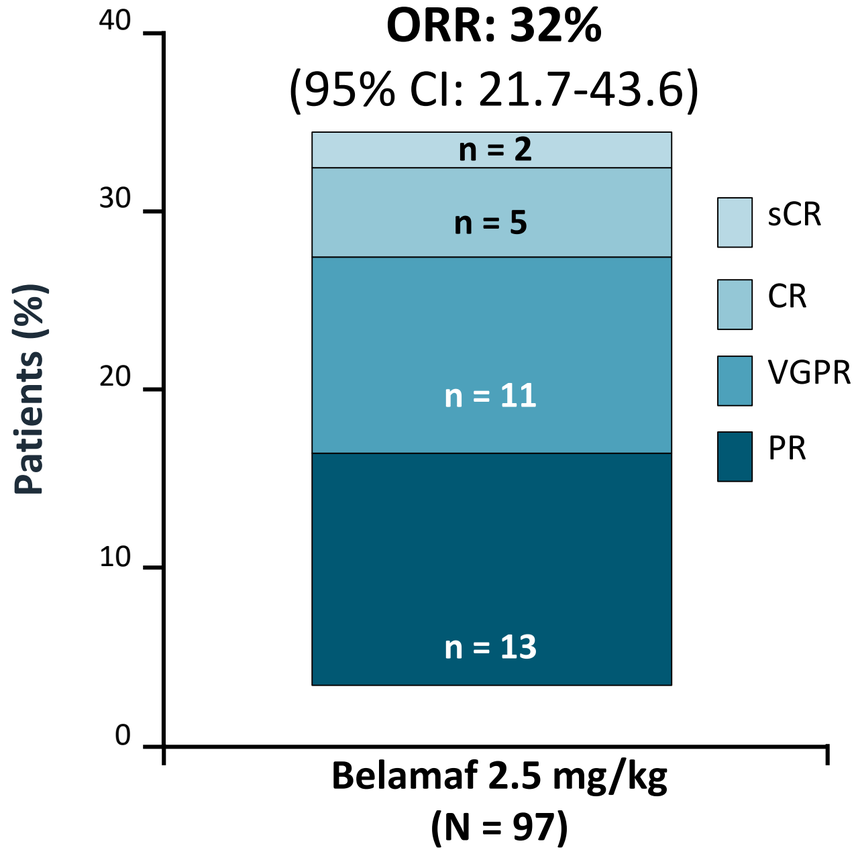


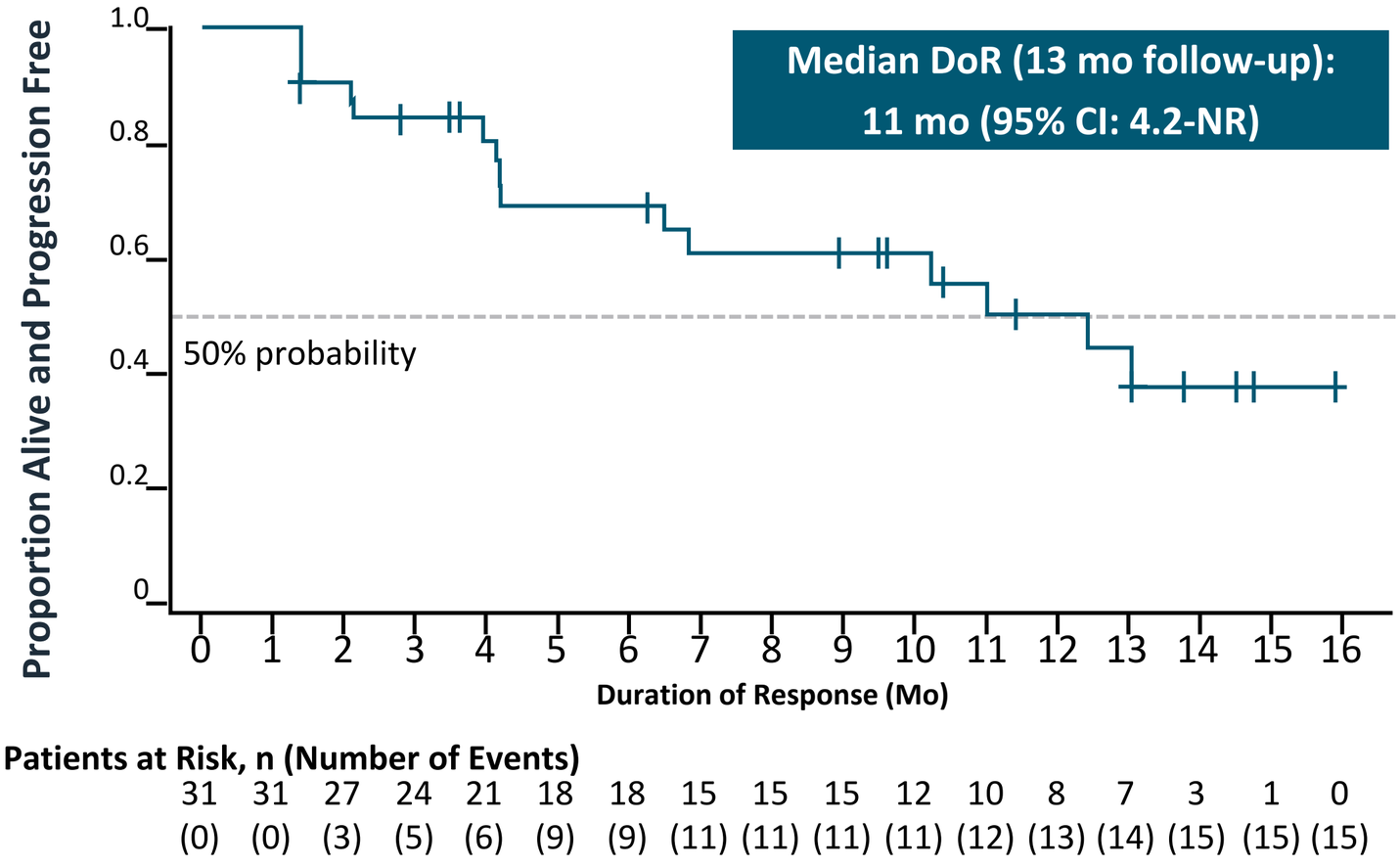
Multimodal Mechanism of Action

1. Competes for binding of natural BCMA ligands.
2. Potentiates Fc region-mediated actions (ADC, ADCC, ADCP)
3. MMAF: microtubule network disruption
4. Immunogenic cell death markers

Tai. Blood. 2014;123:3128. Farooq. Ophthalmol Ther. 2020;9:889.

Response and DoR at 13 Mo of Follow-up





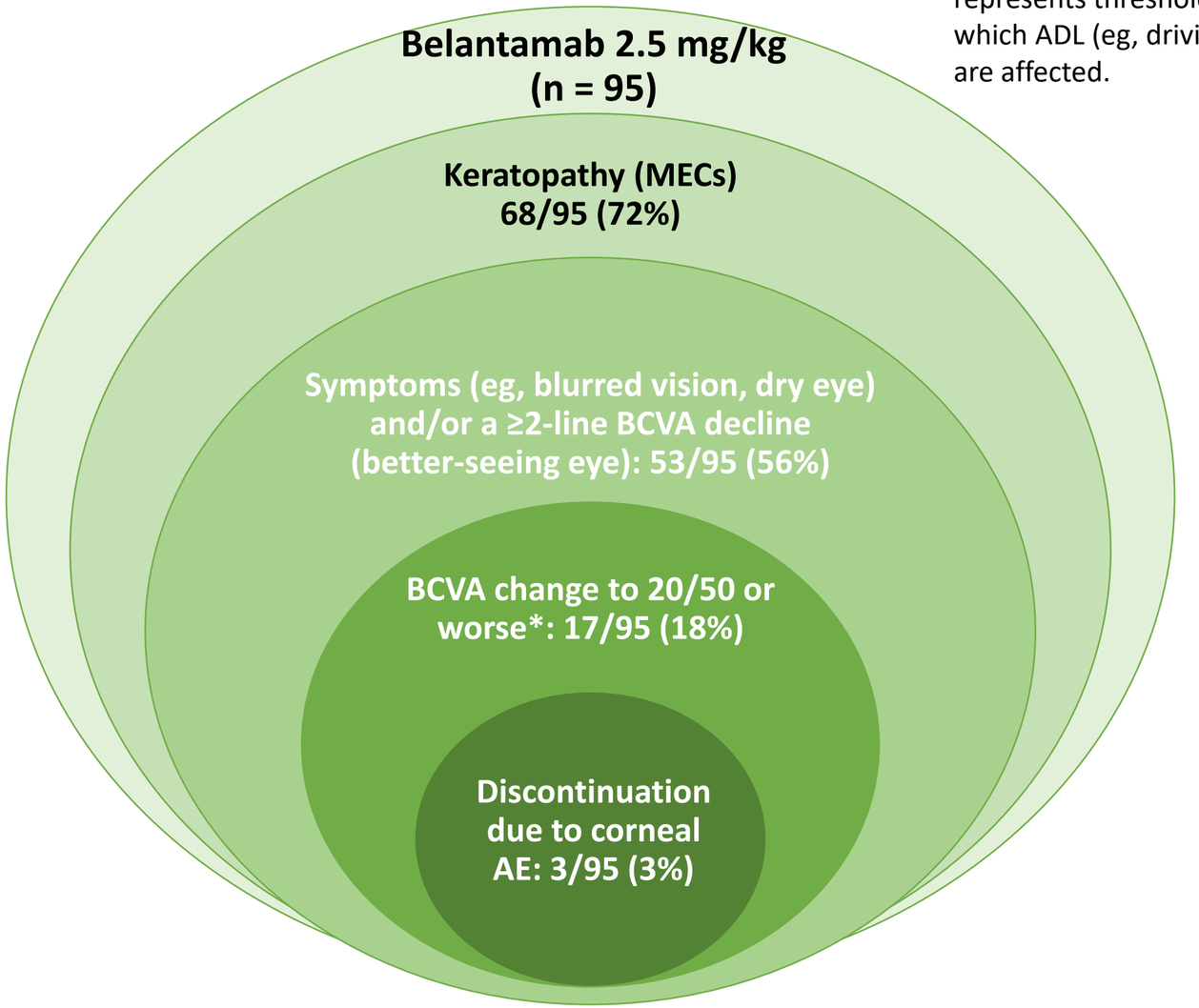
Lonial. Cancer. 2021;127:4198.

Belantamab mafodotin

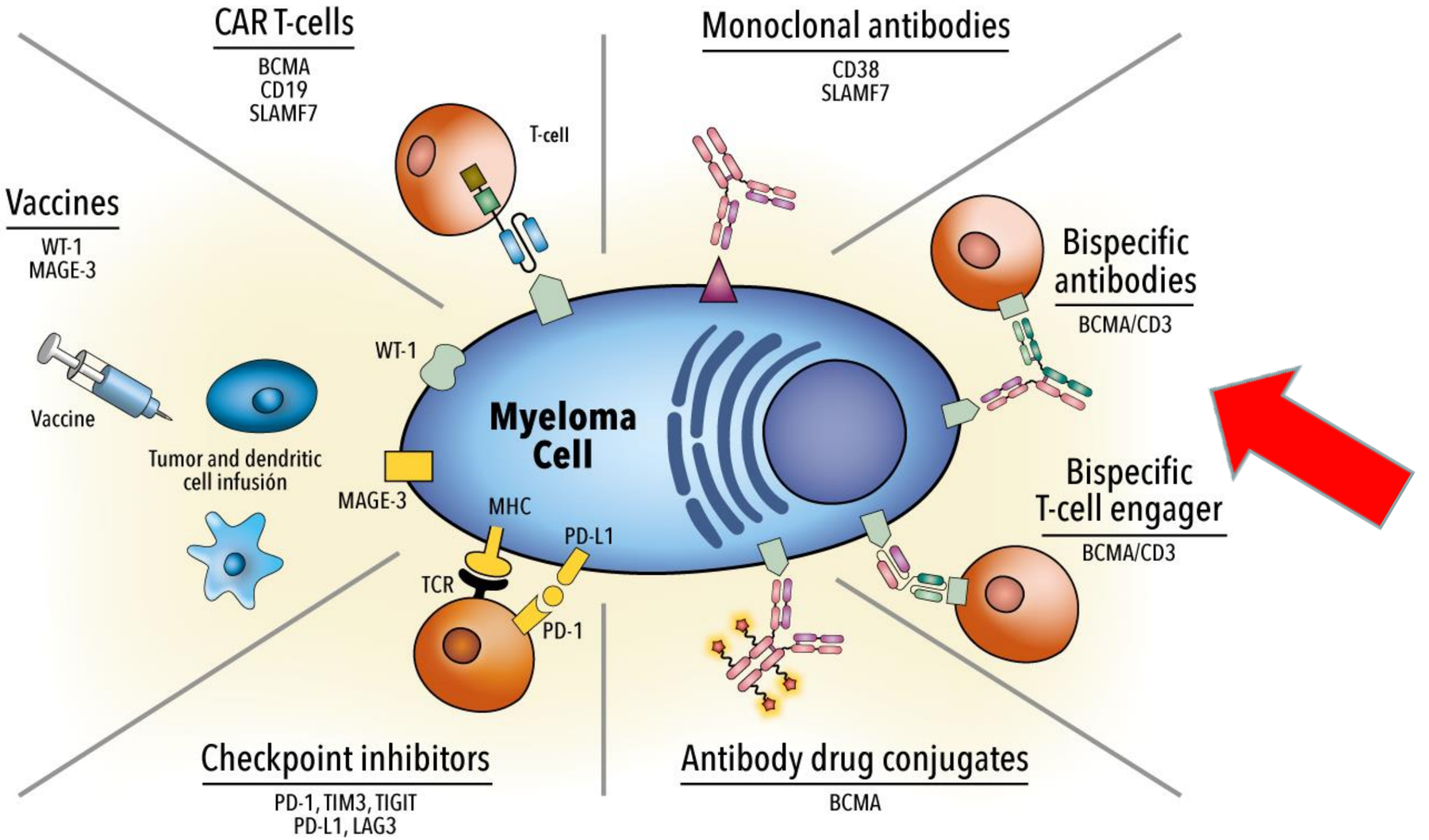
Event	Any Grade	Grade ≥3
Any event	93 (98)	80 (84)
Eye examination finding		
Keratopathy[b]	68 (72)	44 (46)
Change in BCVA	51 (54)	29 (31)
Thrombocytopenia[c]	36 (38)	21 (22)
Anemia	26 (27)	20 (21)
Blurred vision[d]	24 (25)	4 (4)
Nausea	24 (25)	0 (0)
Pyrexia[e]	22 (23)	4 (4)
Aspartate aminotransferase increased	20 (21)	2 (2)
Infusion-related reaction[f]	20 (21)	3 (3)
Fatigue	15 (16)	2 (2)
Neutropenia[g]	14 (15)	10 (11)
Dry eye[h]	14 (15)	1 (1)
Hypercalcemia	14 (15)	7 (7)
Lymphocyte count decreased	13 (14)	12 (13)
Pneumonia	9 (9)	6 (6)

- **Visual acuity changes are time limited**
  - Dose modifications allow continued therapy
  - After grade 3/4 event, 84% of patients' vision returned to baseline or near baseline at last follow-up
  - Partnership with ophthalmologist is required through REMS

*Better-seeing eye; represents threshold at which ADL (eg, driving) are affected.

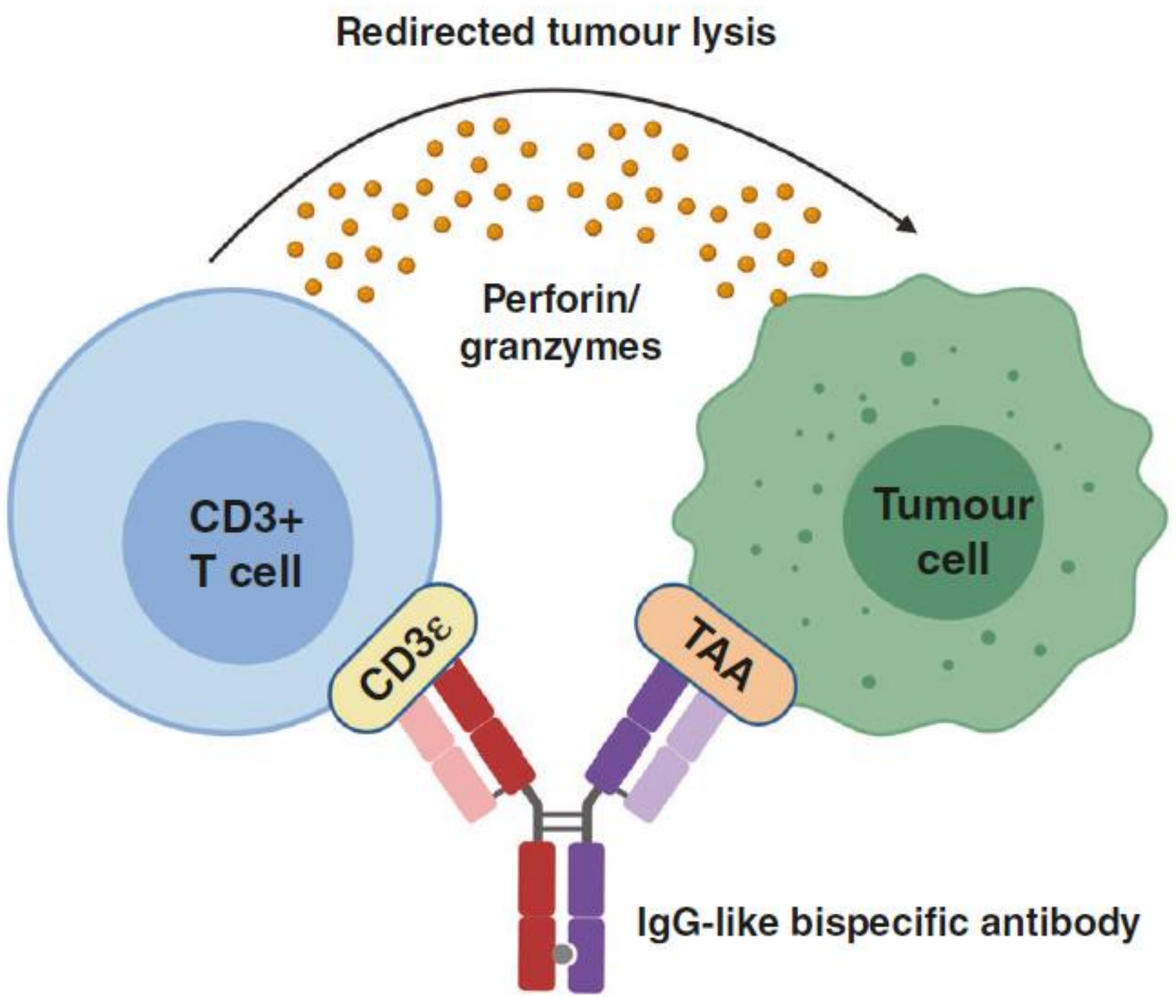


Lonial S, et al. Cancer. 2021
Wahab A, et al. Front Oncol. 2021



Rodriguez-Lobato *et al*. Hemato 2020

Bispecific Antibodies: Mechanism of Action



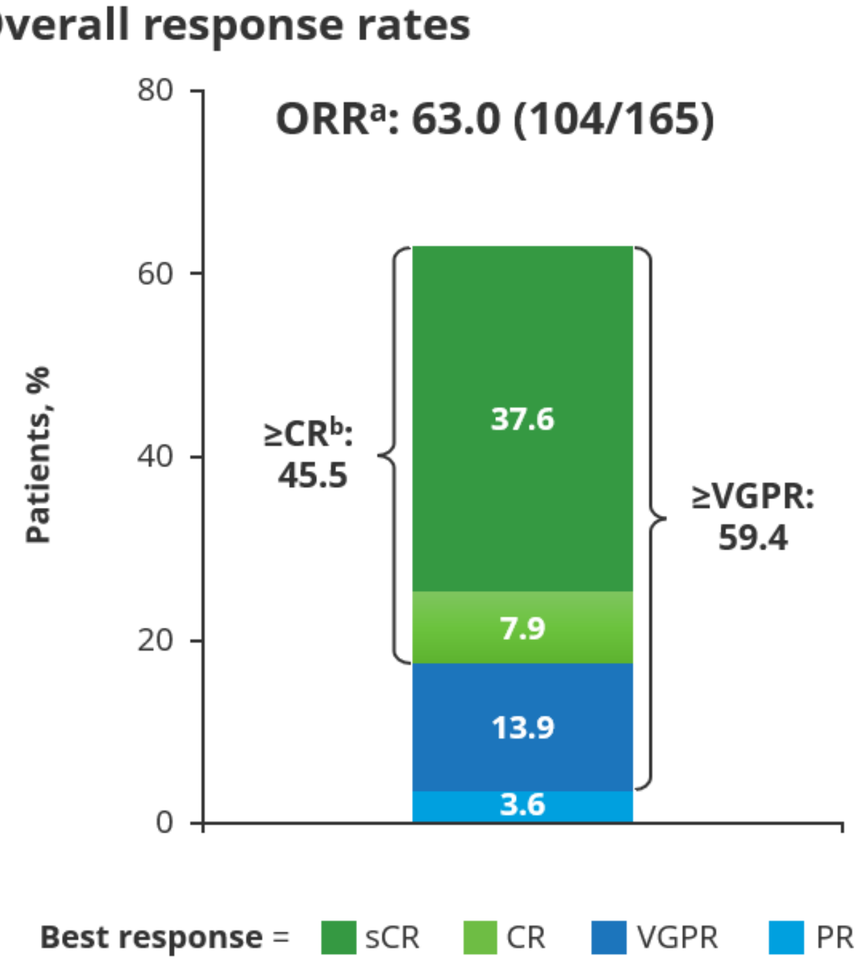
CD3 bispecifIc T-cell redirection mechanism of action in cancer immunotherapy

Singh A, et al. Br J Cancer. 2021

MajesTEC-1: Phase I/II

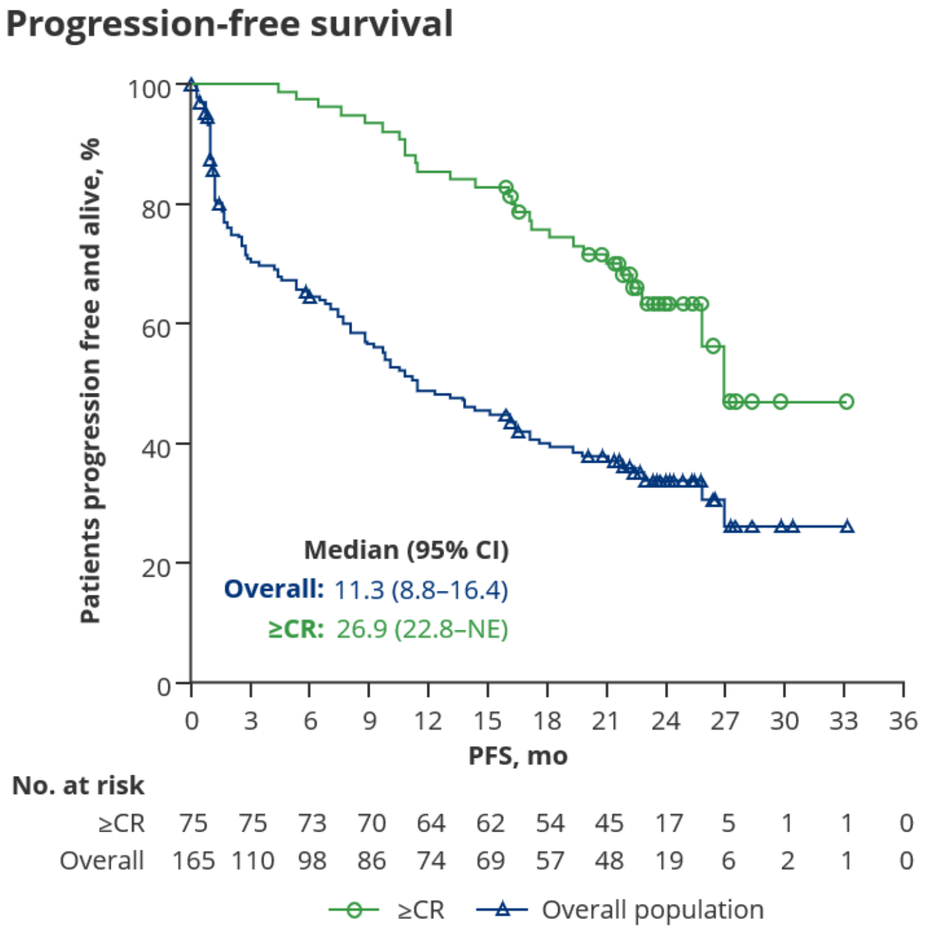
- **Patients with R/R MM after ≥3 lines of therapy, including exposure to IMiD, PI, and anti-CD38 mAb**
  - 26% high-risk cytogenetics
  - Median 5 prior lines of therapy (range: 2-14)
  - 77.6% triple-class refractory; 30.3% penta-drug refractory
  - 89.7% refractory to last therapy line
- **Teclistamab**: 1.5 mg/kg SC weekly, after step-up

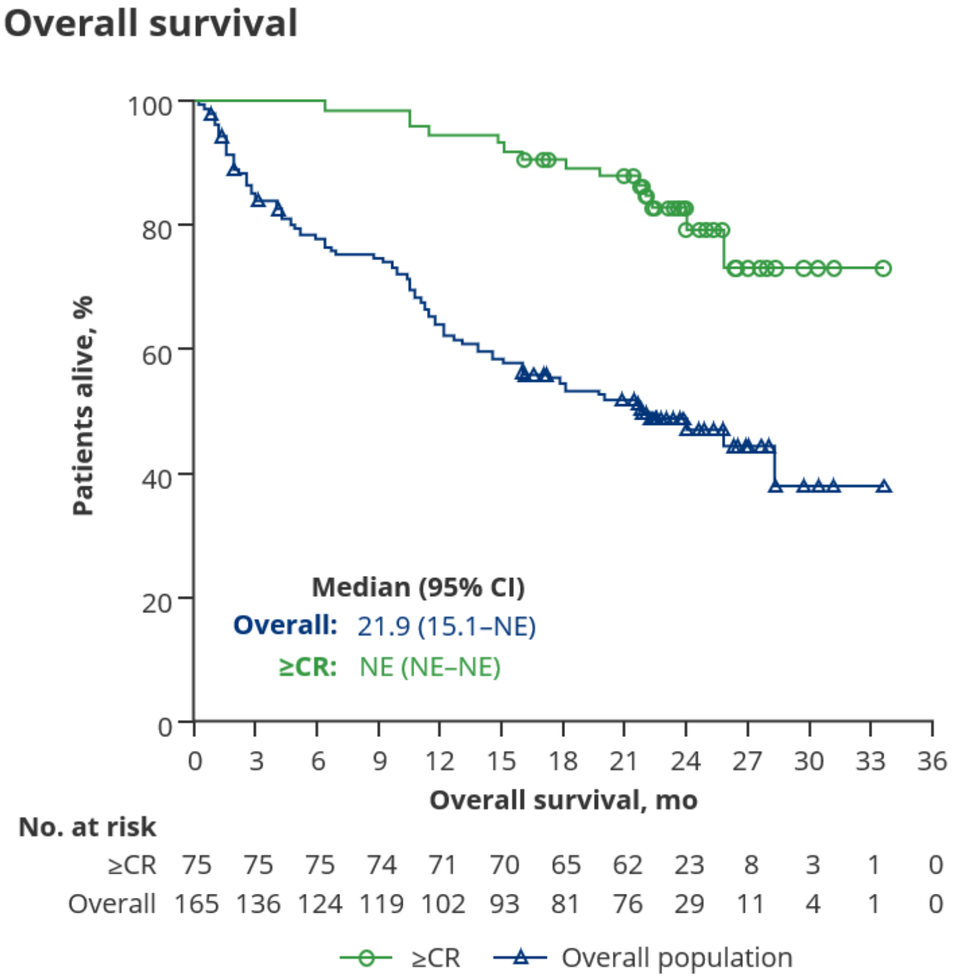
Event	All Patients (N = 165)
MRD negativity at 10^{-5}, n (%; 95% CI)	44 (26.7; 20.1-34.1)
Median DoR, mo (95% CI)	18.4 (14.9-NE)
Median PFS, mo (95% CI)	11.3 (8.8-17.1)
Median OS, mo (95% CI)	18.3 (15.1-NE)



Van de Donk *et al*. ASCO. 2023

MajesTEC-1: Survival





Van de Donk *et al*. ASCO. 2023

MajesTEC-1: Cytokine-Release Syndrome and Neurotox

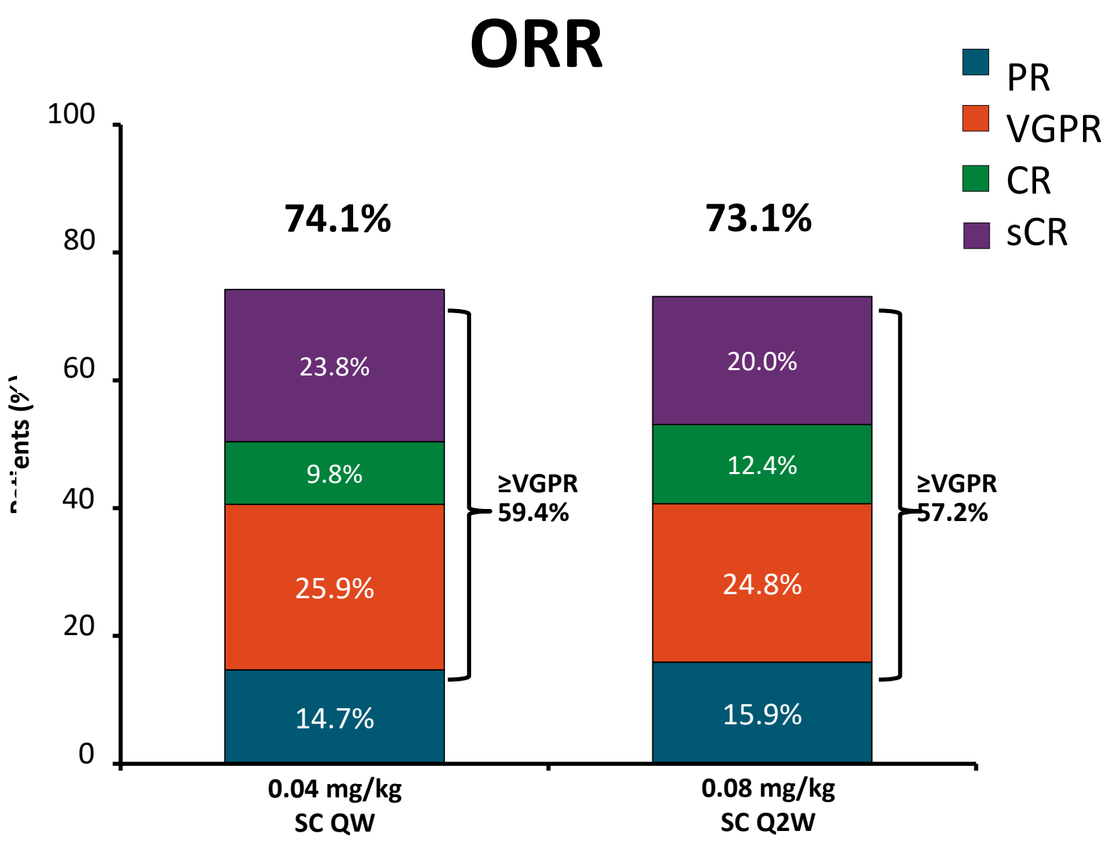
CRS Parameter	All Patients (N = 165)
CRS, n (%)	**119 (72.1)**
≥2 CRS events, n (%)	55 (33.3)
Median time to onset, days (range)	2 (1-6)
Median duration, days (range)	2 (1-9)
Supportive measures, n (%)*	110 (66.7)
▪ Tocilizumab	60 (36.4)
▪ Low-flow oxygen by nasal cannula†	21 (12.7)
▪ Corticosteroids	14 (8.5)
▪ Single vasopressor	1 (0.6)

Neurotox Parameter	All Patients (N = 165)
Neurotox, n (%)	**21 (12.7)**
≥3 Neurotox events, n (%)	0
Median time to onset, days (range)	2.5 (1-7)
Median duration, days (range)	3 (1-37)
Supportive measures, n (%)*	12 (7.3)
▪ Tocilizumab	3 (1.8)
▪ Dexamethasone	3 (1.8)
▪ Levetiracetam	1 (0.6)

*Patients could receive >1 supportive measure. †≤6 L/min.

Nooka et al. ASCO 2022. Abstr 8007; Moreau *et al*. NEJM. 2022;387:495.

MonumenTAL-1 Phase I Trial



- Similar ORR among all subgroups, 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

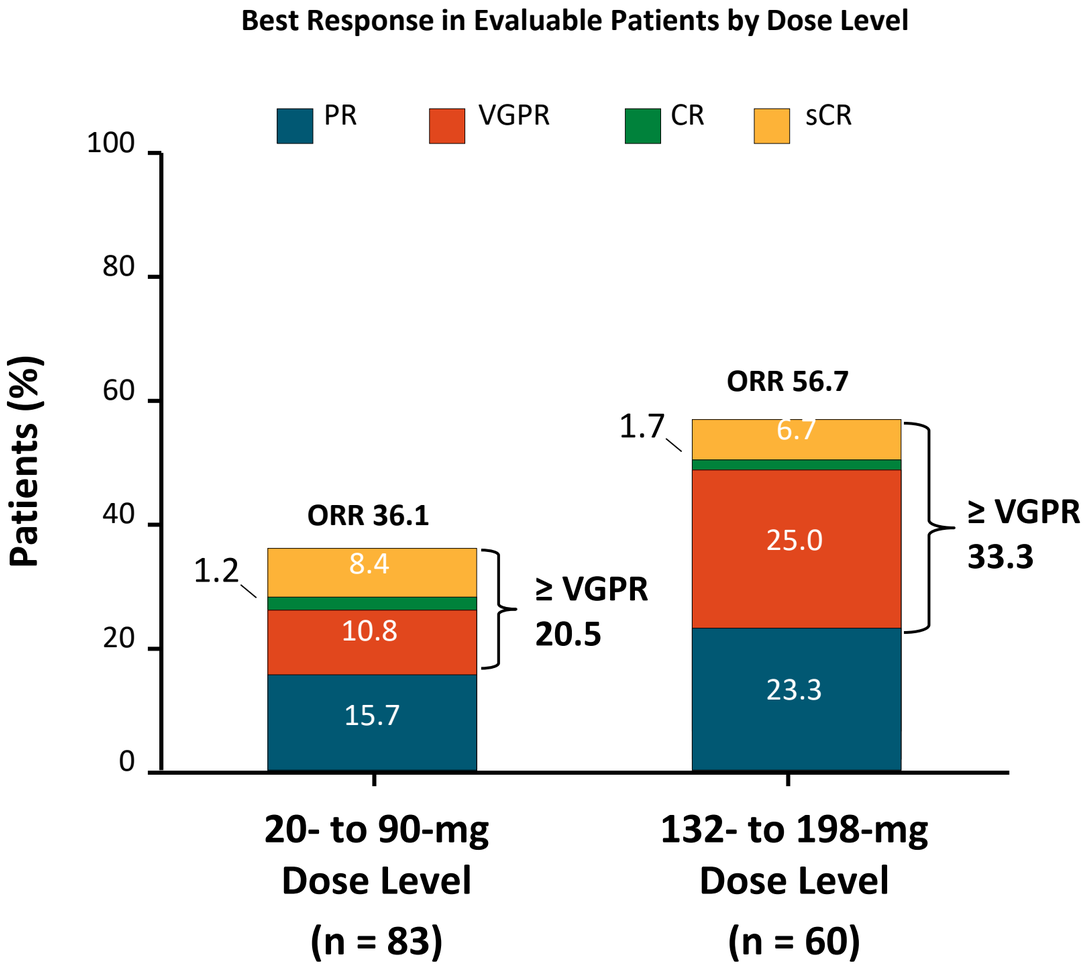
Timing	0.4 mg/kg SC QW (n = 143)	0.8 mg/kg SC Q2W (n = 145)
Median follow-up for efficacy, mo (range)	14.9 (0.5-29.0)	8.6 (0.2-22.5)
Median time to first response, mo (range) (n = 106 in each group)	1.2 (0.2-10.9)	1.3 (0.2-9.2)
Median time to best response, mo (range) (n = 106 in each group)	2.2 (0.8-12.7)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

Chari *et al*. ASH 2022. Abstr 157.

Cevostamab in RR/MM

- Responses occurred at and above 20-mg target dose level (n = 143)
- ORR increased with target dose
  - ORR in C1 single step-up expansion (3.6 mg/90 mg): 29.0%
  - ORR in C1 double step-up expansion (0.3 mg/3.6 mg/160 mg): 54.8%

Outcome	Cevostamab (N = 161)
Median time to response among responders, mo (range)	1.0 (0.7-5.9)
Median time to best response, mo (range)	2.1 (0.7-11.4)
MRD negativity at $<10^{-5}$ in patients with ≥ VGPR, n/N (%)	7/10 (70)
Median duration of response in C1 step-up cohort, mo (95% CI)	11.5 (6.0-18.4)



Trudel *et al*. ASH 2021. Abstr 157.

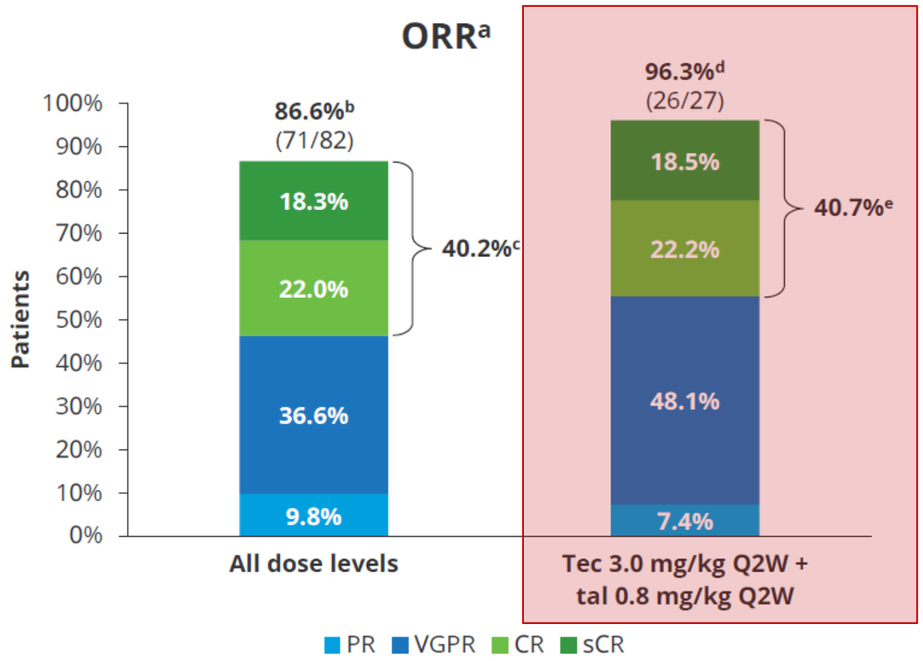
Bispecific antibodies in Multiple Myeloma

	Teclistamab (n=165)	Linvoseltamab (n=73)	ABBV-383 (n=118)	Elranatamab (n=123)	Alnuctamab (n=68)	Talquetamab (n=288)		Forimtamag (n=51 / 57)	Cevostamab (n=157)
Target	**BCMA**	**BCMA**	**BCMA**	**BCMA**	**BCMA (2+1)**	**GPRC5D**		**GPRC5D**	**FcRH5**
Route	SC	IV	IV	SC	SC	SC	SC	IV / SC	IV
Dose and schedule	1.5 mg/kg/Q1w	Q1w x 17w W≥17: Q2w	Q3w	76 mg/Q1w C≥7: Q2w if PR	Q1w x 8w Q2w C3-C7 C≥7 Q4w	0.4 mg/kg Qw N=143	0.8 mg/kg Q2w N=145	0.006 mg to 10 mg Q2w	Q2w
Median prior LoT	5	5	5	5	4	5	5	5 / 4	6
Triple refractory	78%	89%	61%	96%	63%	74%	69%	62% / 72%	85%
CRS, G≥3	72%, 0.6%	38%, 0%	54%, 3%	58%, 0%	53%, 0%	79%, 2%	72%, 0.7%	82% / 2%	81%, 1%
Neurotoxicity, G≥3	3%, 0%	4%, 0%	NR, 6 pts	4%, 3%	2 pts, 3%	14%, 2%	10%, 2%	11%	14%, 0.6%
ORR	63%	75% 200-800 mg	60%/81% At ≥40 mg	61%	53%	74%	73%	68%	57% 132-198 mg
≥CR	39%	16%	20%/30%	28%	23%	34%	32%	35% / 26%	8%
Median PFS	11 m	NR	NR	15m: 51%	NR	7.5	11.9	NR	NR
Median OS	22 m	NR	NR	15m: 72%	NR	9	13	NR	12
MRD – (10^{-5})	27%	4/10	NR	91%	16/20	NR	NR	NR	7/10

Combination Therapy

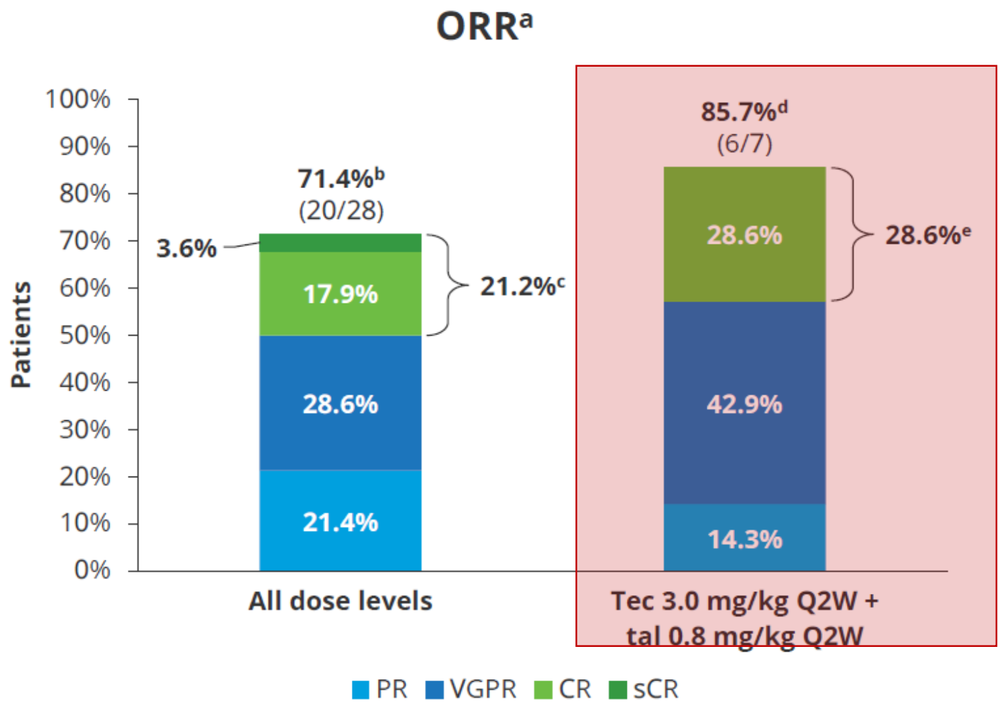
Teclistamab + Talquetamab: RedirecTT-1 study

- **Median prior LOT: 4** (2-10)
- Exrramedullary disease: 38%
- Triple-class refractory: 80%



9-m PFS 77%

Extramedullary Disease



mPFS 10 months

Mateos MV, et al. EHA. 2023

CAR-T cells vs. bispecifics

	CAR-T[1,2]	Bispecific antibodies[3,4]
Availability	6-10 weeks	Off the shelf
Age	61 (33-78)	64-69 (33-89)
Administration	IV one shot	SC until PD
CRS ≥ grade 3	5-9%	1%
Neurotoxicity ≥ grade 3	6-10%	0%
ORR	82-98%	60-63% RP2D
Median PFS	12 to >27 mos	11.3 mos

CAR-T, chimeric antigen receptor T-cell therapy; CRS, cytokine release syndrome; ORR, overall response rate; PD, progressive disease; RP2D, recommended phase 2 dose; SC, subcutaneous

1. Munshi N, *et al*. ASCO 2020; 2. Usmani S, *et al*. ASCO 2022;
3. Nooka A, *et al.* ASCO 2022; 4. Lesokhin AM, *et al.* ASCO 2022

CAR-T cells vs. bispecifics

	CAR-T[1,2]	Bispecific antibodies[3,4]
Availability	6-10 weeks	Off the shelf
Age	61 (33-78)	64-69 (33-89)
Administration	IV one shot	SC until PD
CRS ≥ grade 3	5-9%	1%
Neurotoxicity ≥ grade 3	6-10%	0%
ORR	82-98%	60-63% RP2D
Median PFS	12 to >27 mos	11.3 mos

CAR-T, chimeric antigen receptor T-cell therapy; CRS, cytokine release syndrome; ORR, overall response rate; PD, progressive disease; RP2D, recommended phase 2 dose; SC, subcutaneous

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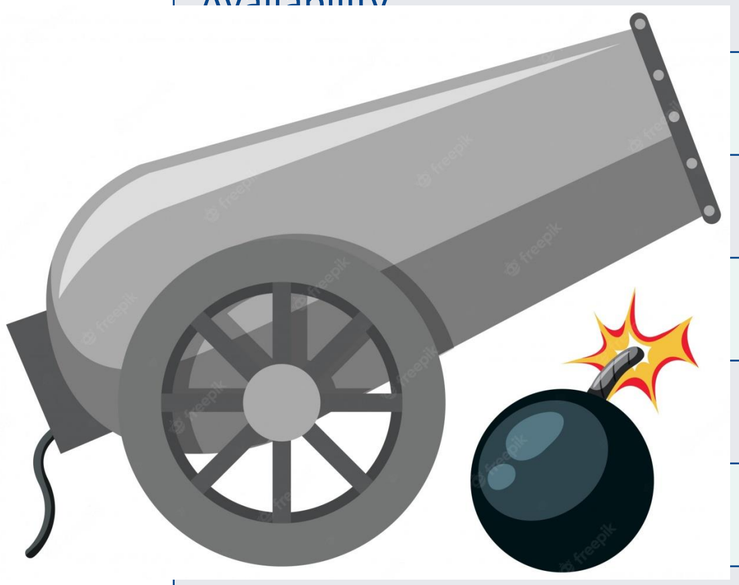
CAR-T cells vs. bispecifics

	CAR-T[1,2]	Bispecific antibodies[3,4]
Availability	6-10 weeks	Off the shelf
	61 (33-78)	
	IV one shot	
Median PFS	12 [illegible]mos	11.5 mos



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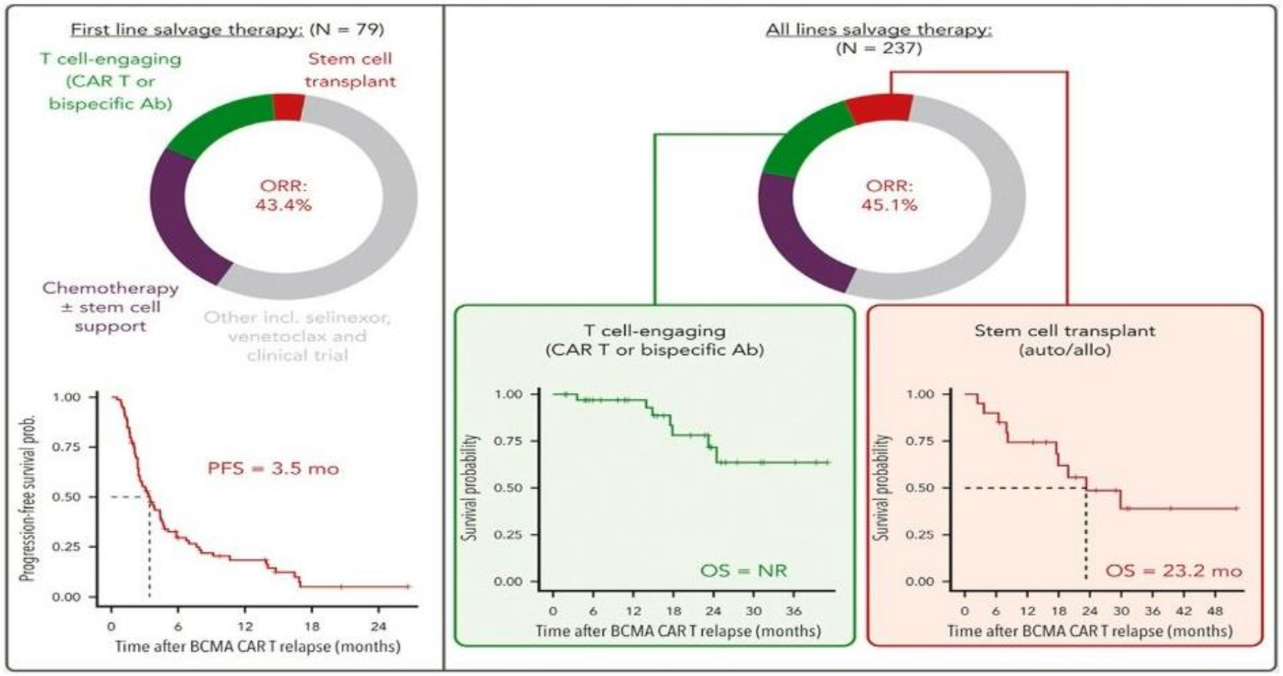
Optimal sequencing of BCMA therapies

-Median PFS of patients transitioning to bispecific antibody therapy immediately after CAR T was not yet reached.

- Changing the target?
  GPRC5D, FcRH5

Salvage with TCE or ASCT has better outcome



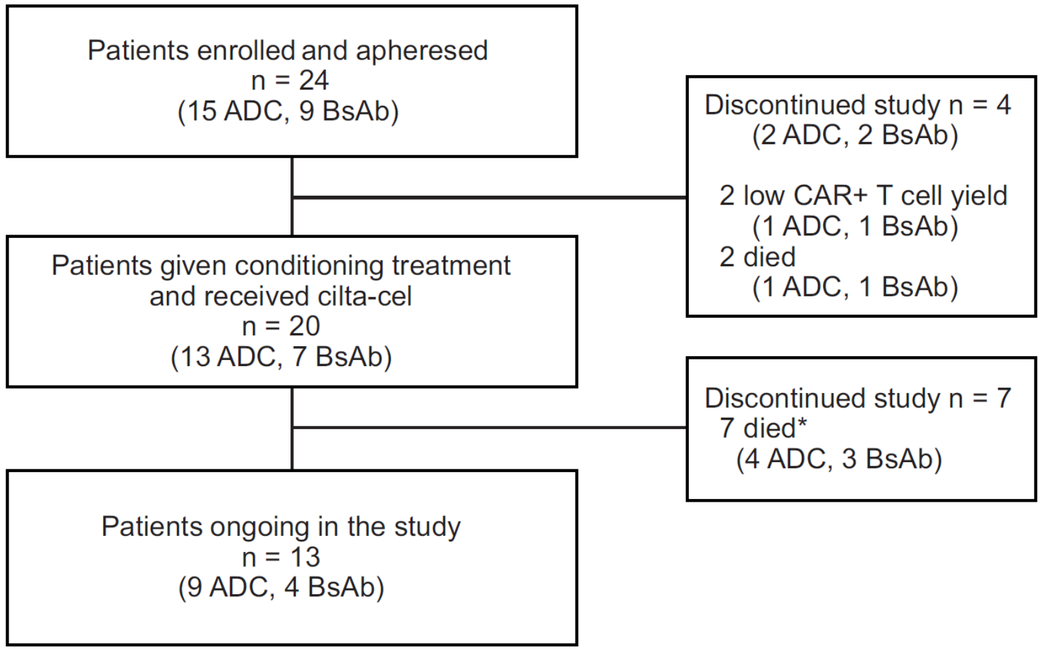
In collaboration with MSKCC (Sham Mailankody et al)

Van Oekelen et al, Blood 2023

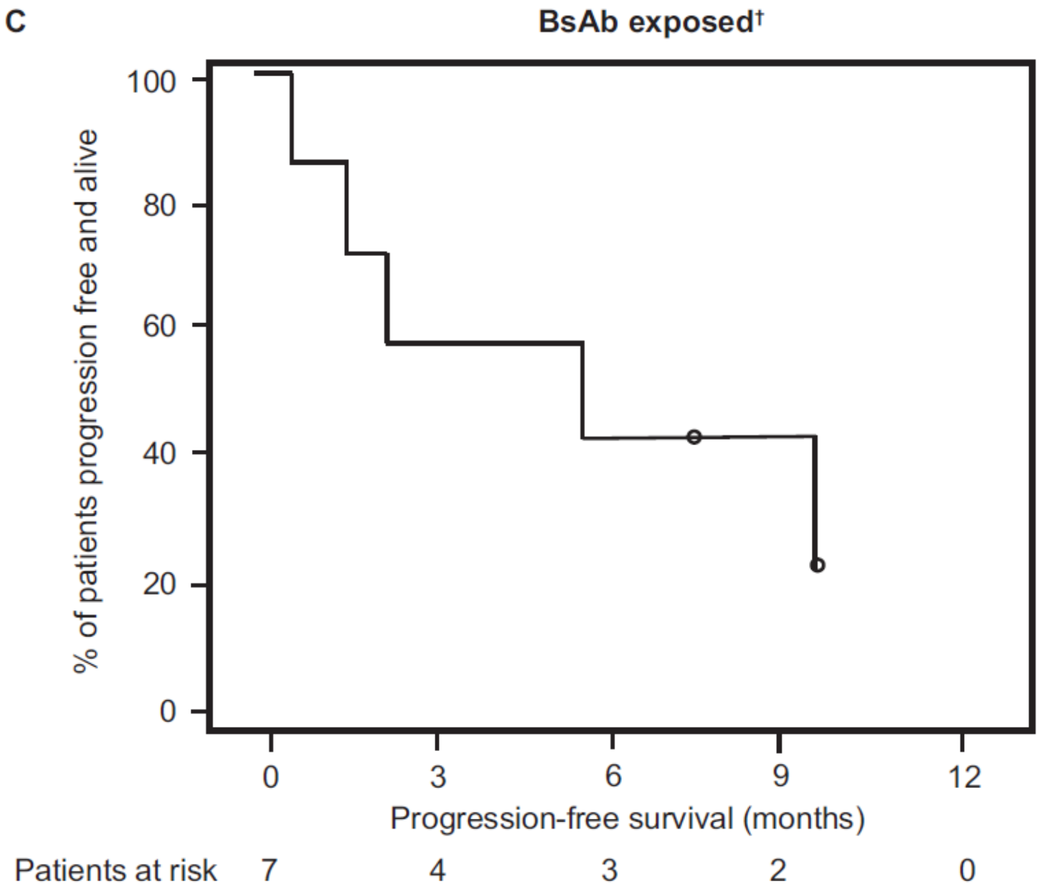
Sequencing T-cell redirection therapies leads to deep and durable responses in relapsed/refractory myeloma patients

Mouhieddine *et al*. Blood Adv 2022

Optimal sequencing of BCMA therapies



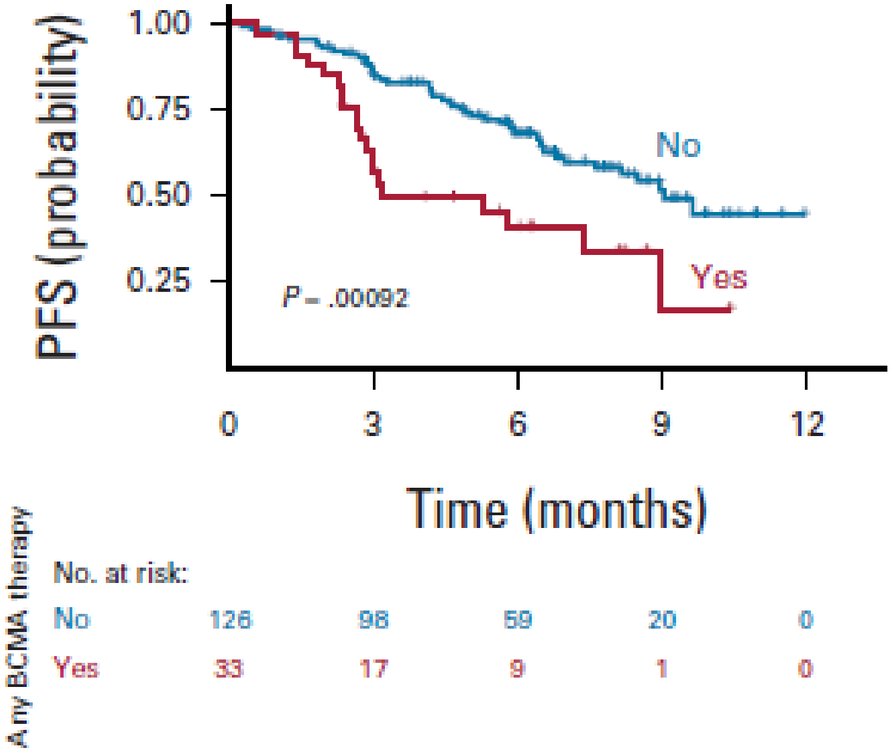
- Overall response rate was 60.0%
- Median duration of response 11.5 months
- Median PFS 9.1 months



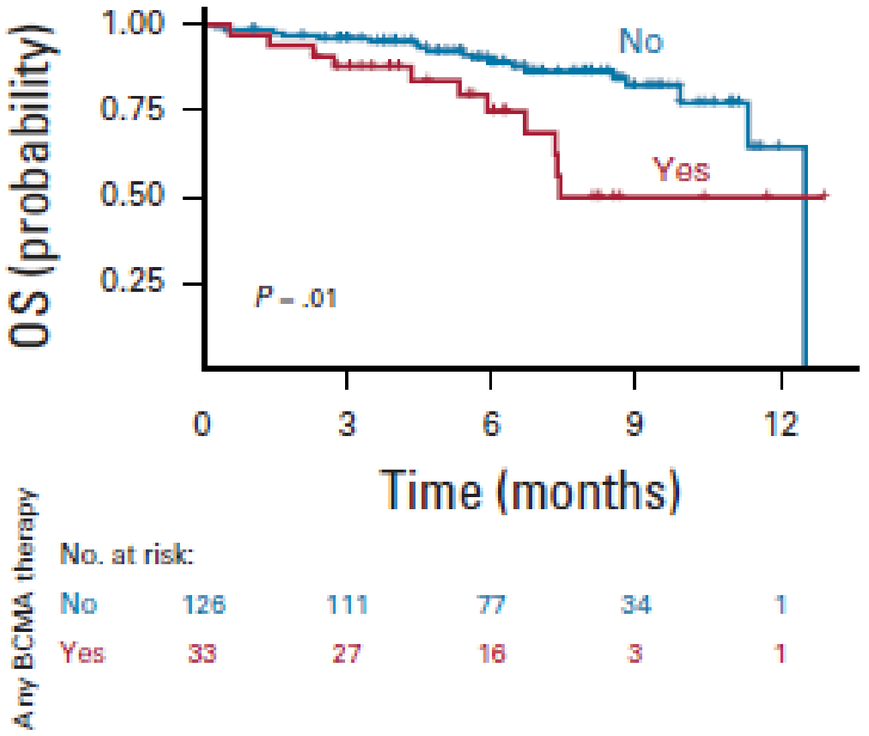
PRIOR BCMA THERAPY MATTERS

Cohen *et al*. Blood 2022

Ide-cel in real world experience: Myeloma CAR-T consortium



No BCMA therapy: Median PFS, 9.0 months (95% CI, 7.6 to NR)
BCMA therapy: Median PFS, 3.2 months (95% CI, 2.8 to NR)

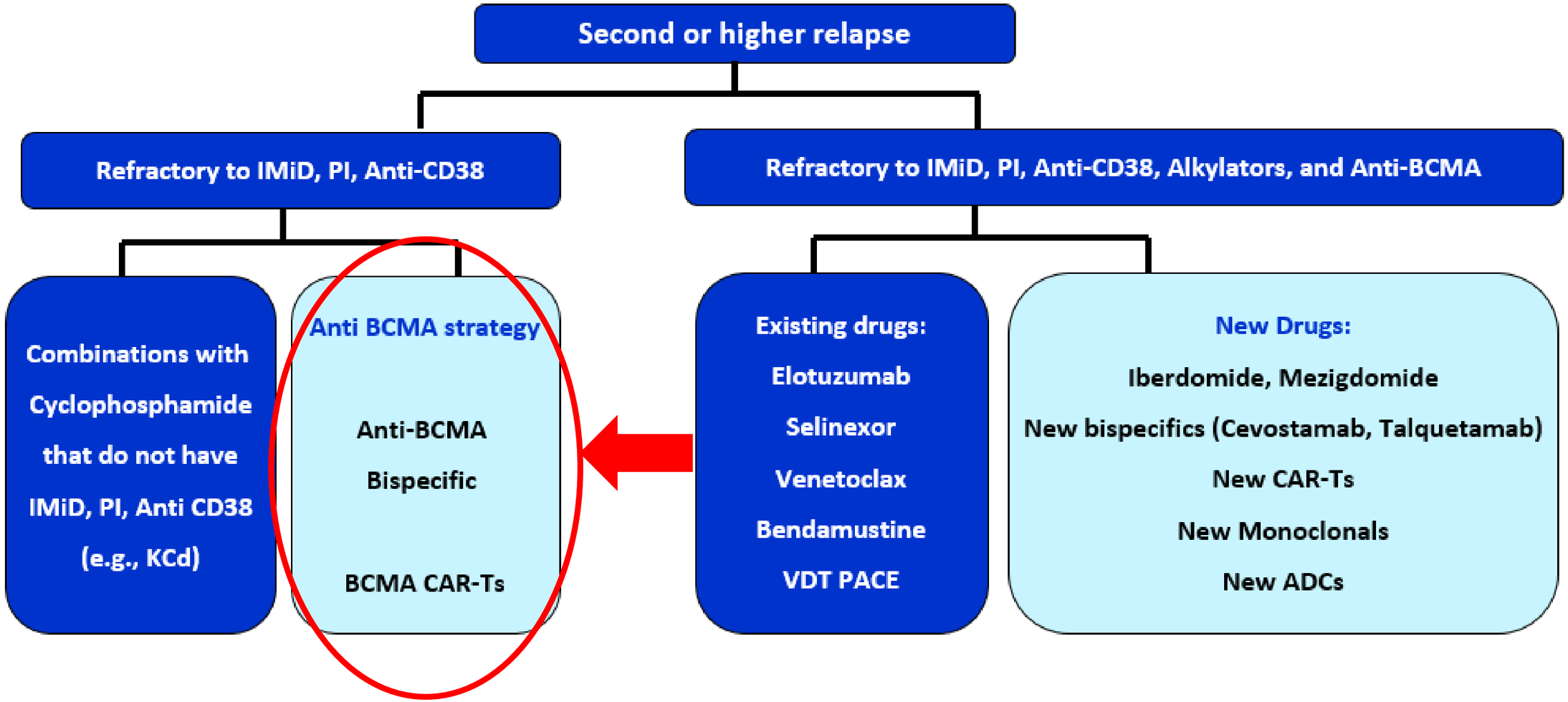


No BCMA therapy: Median OS, 12.5 months (95% CI, 11.3 to NR)
BCMA therapy: Median OS, 7.4 months (95% CI, 7.3 to NR)

PRIOR BCMA THERAPY MATTERS

Hansen *et al*. JCO 2023

Myeloma: Second or higher relapse



How to Choose the Best Anti-BCMA Therapy?

	CAR T-Cell	Bispecific mAbs	ADCs
Convenience	- - - - Specialized center, Caregiver needed **Manufacturing**	+ + + **Off the shelf,** **Community friendly (?)**	+ + **Off the shelf** **Community friendly**
Length of treatment	+ + + + + + 1-time administration	- - Ongoing	- - Ongoing
ORR	**73-98%**	65-85%	32%
PFS	**>9 months**	11 months	3 months
Toxicities	**CRS, neurotoxicity**, cytopenias, infection	CRS, cytopenias, **infection**	**Corneal microcysts**, thrombocytopenia
Cost	-/+ >$400K	**-/+** But have to consider length of treatment	**++** $24K/mo

In practice: currently we choose what is available at "that specific time"

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ISCIII

Instituto de Salud Carlos III

"la Caixa" Foundation

asociación española contra el cáncer

ISCIII Terav

Red Española de Terapias Avanzadas - TerCel

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