GIORNATE EMATOLOGICHE VICENTINE

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12-13 Ottobre 2023
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Car-T e mieloma: quali pazienti, in che fase di malattia

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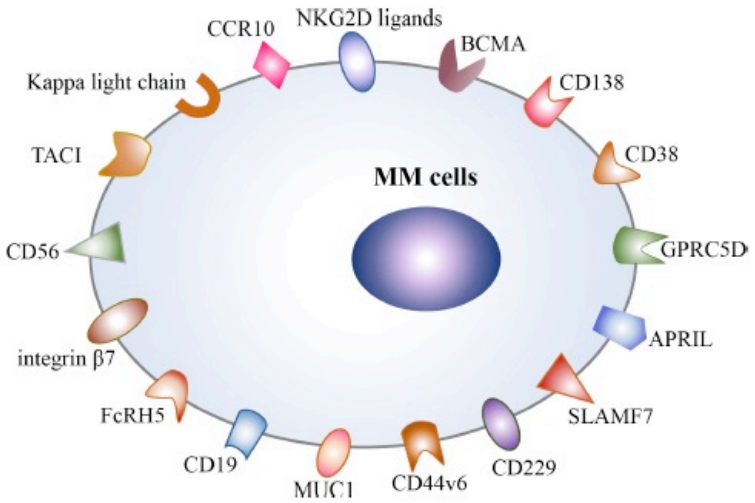
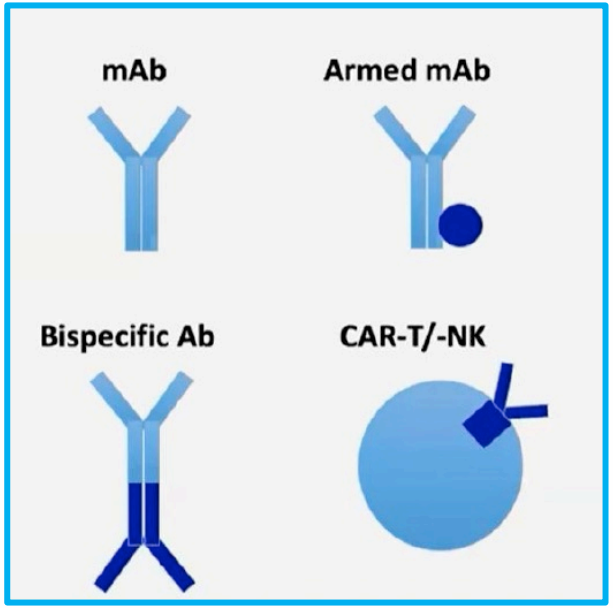
Disclosures of Patrizia Chiusolo

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Astellas					x		
BMS					x		
Novartis					x		
GSK					x		
MSD					x		

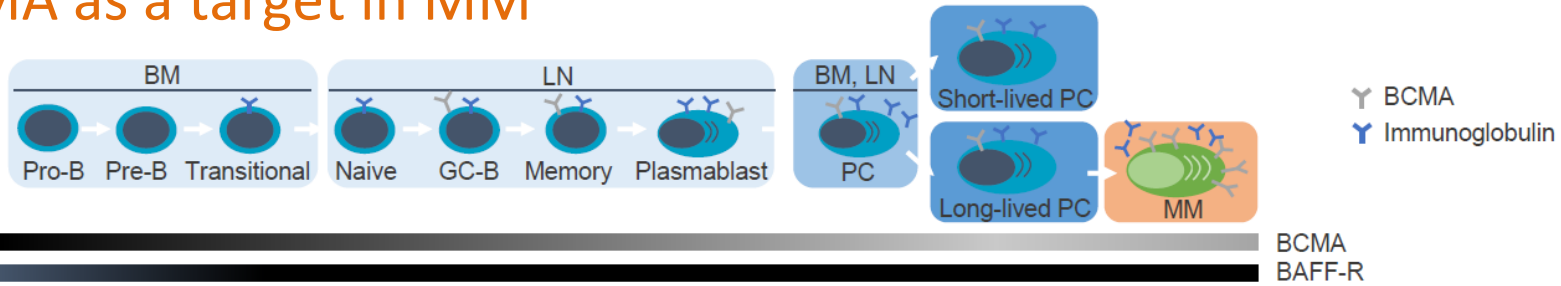
Potential therapeutic targets in MM

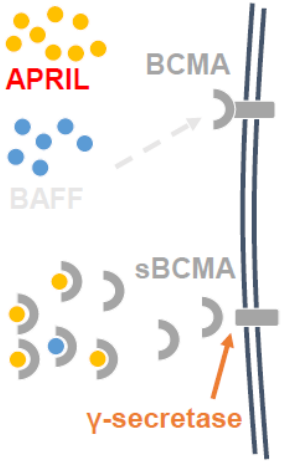




Zhang X et al, Front Immunology 2023

BCMA as a target in MM



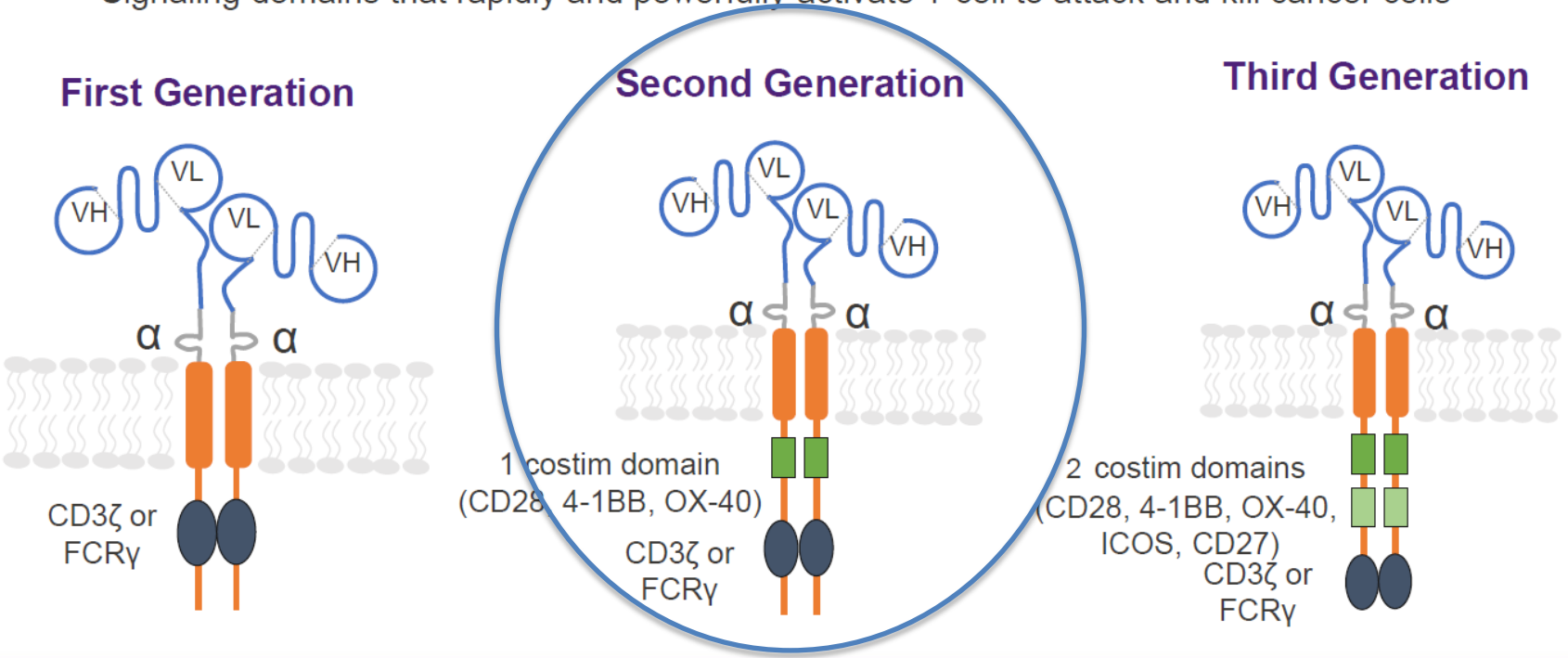


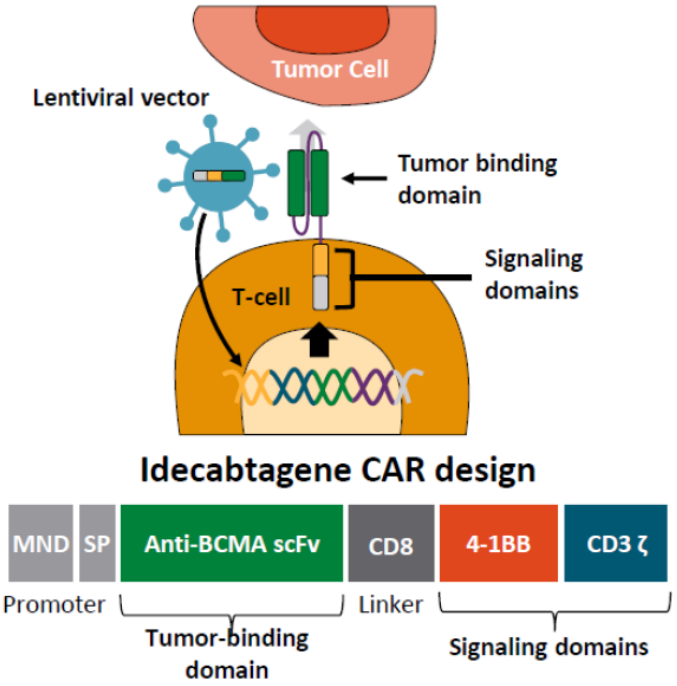
- BCMA: Antigen expressed specifically on PCs and myeloma cells
- Cell-surface receptor in TNF superfamily
- Higher expression on myeloma cells than normal PCs
- Not expressed in other tissues
- Key role in B-cell maturation and differentiation
- Promotes myeloma cell growth, chemotherapy resistance, immunosuppression in bone marrow microenvironment
- Expression of BCMA increases with progression from MGUS to advanced myeloma
- Additional ligands for BMCA include APRIL and BAFF

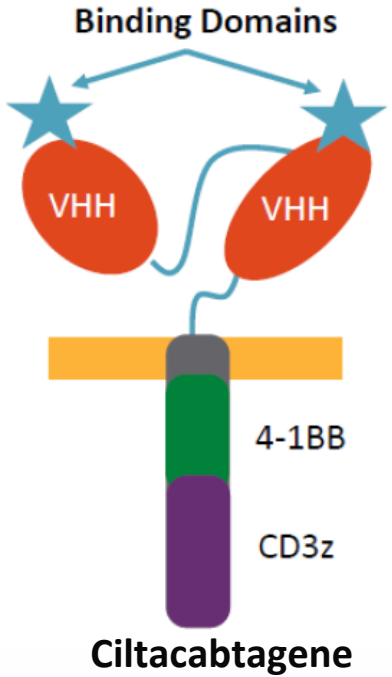
Cho. Front Immunol. 2018;9:1821. Moreaux. Blood. 2004;103:3148. Sanchez. Br J Haematol. 2012;158:727.

CAR-T cell technology

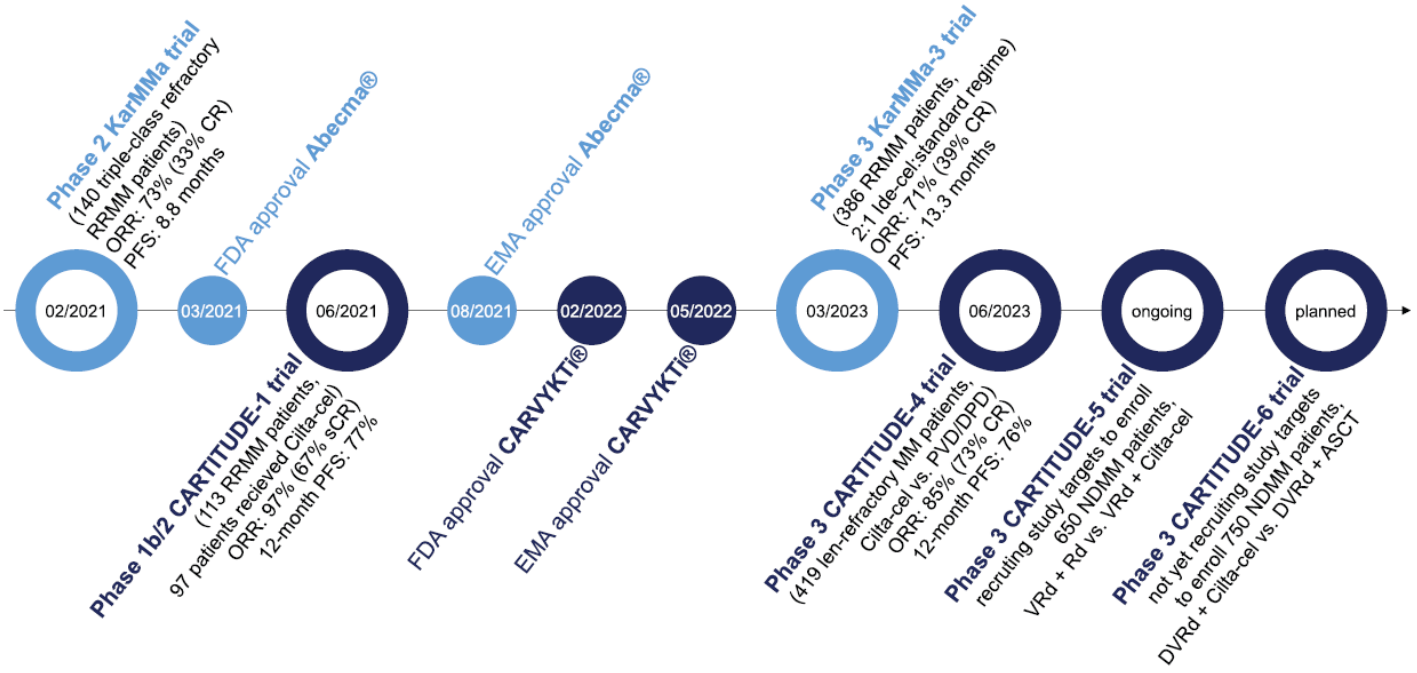
- CARs: Engineered transmembrane receptors with 2 functional components:
  - Antibody fragment or target-binding domain that recognizes targets on the surface of cancer cells
  - Signaling domains that rapidly and powerfully activate T-cell to attack and kill cancer cells




Tumor Cell
Lentiviral vector
Tumor binding domain
Signaling domains
T-cell
Idecabtagene CAR design
MND
SP
Anti-BCMA scFv
CD8
4-1BB
CD3 ζ
Promoter
Linker
Tumor-binding domain
Signaling domains


Binding Domains
VHH
VHH
4-1BB
CD3z
Ciltacabtagene

Timeline for the Food and Drug Administration (FDA) and European Medicines Agency (EMA) approved CAR T cell therapies in RRMM.



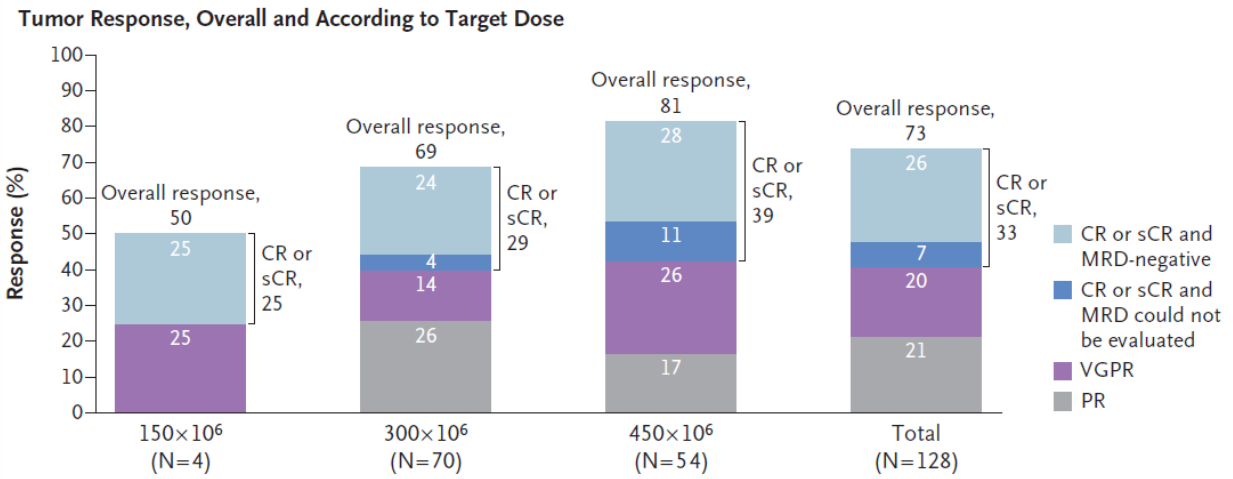
BCMA-Targeted Therapy	Indications	AIFA status
Idecabtagene vicleucel	▪ **Adults with R/R multiple myeloma after ≥3 prior lines of therapy**, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal Ab	▪ Pending in 2023
Ciltacabtagene autoleucel	▪ **Adults with R/R multiple myeloma after ≥3 prior lines of therapy**, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal Ab	▪ Pending in 2024

KarMMa-study

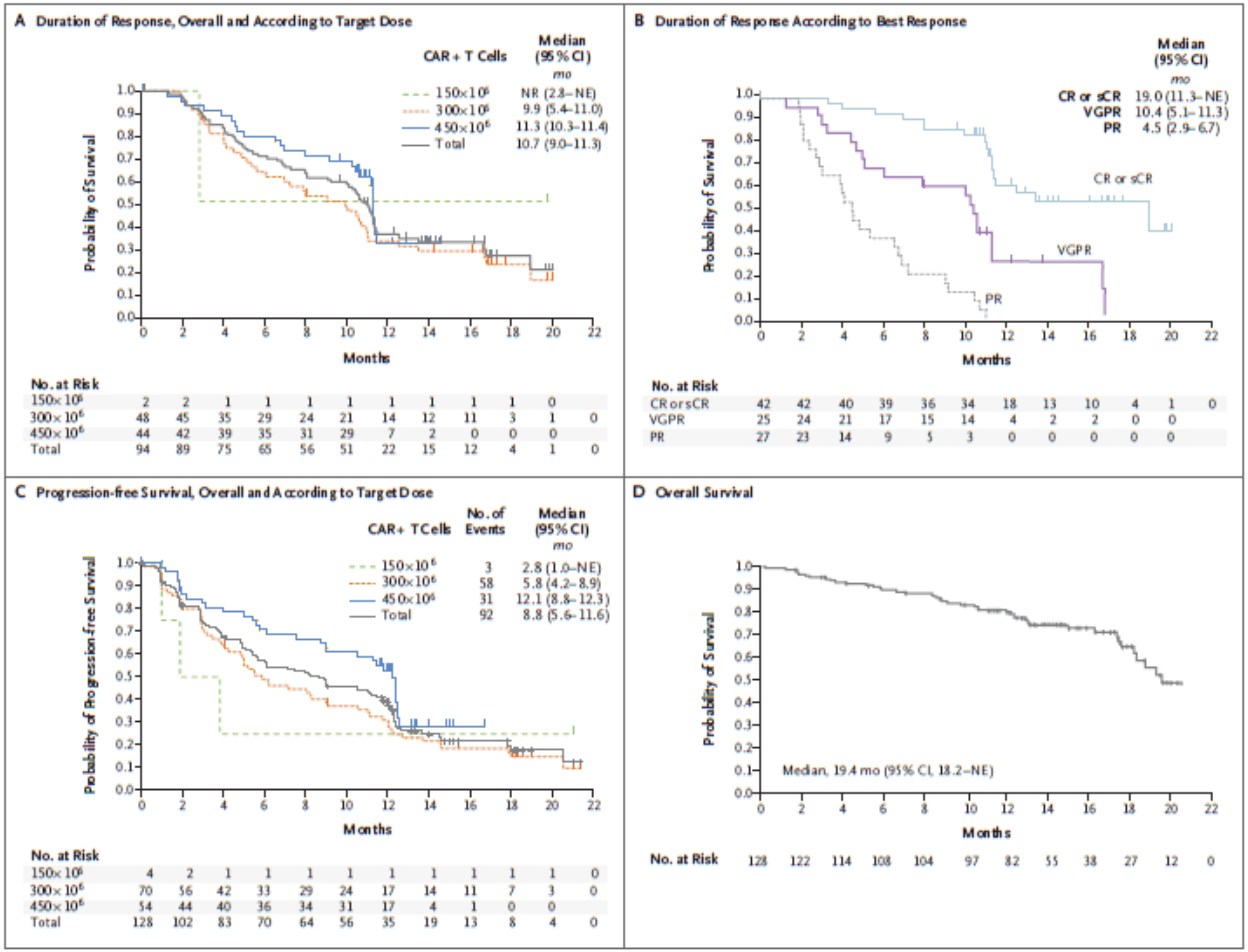
Patients with R/R MM and ≥3 prior regimens each with ≥2 consecutive cycles, prior IMiD, PI, and anti-CD38 mAb, and refractory to last therapy by IMWG criteria (N = 158)

Baseline characteristics:

- High-risk cytogenetics: 35%
- Extramedullary disease: 39%
- Median no. of prior therapies: 6 (range: 3-16)
- Triple refractory: 84%



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

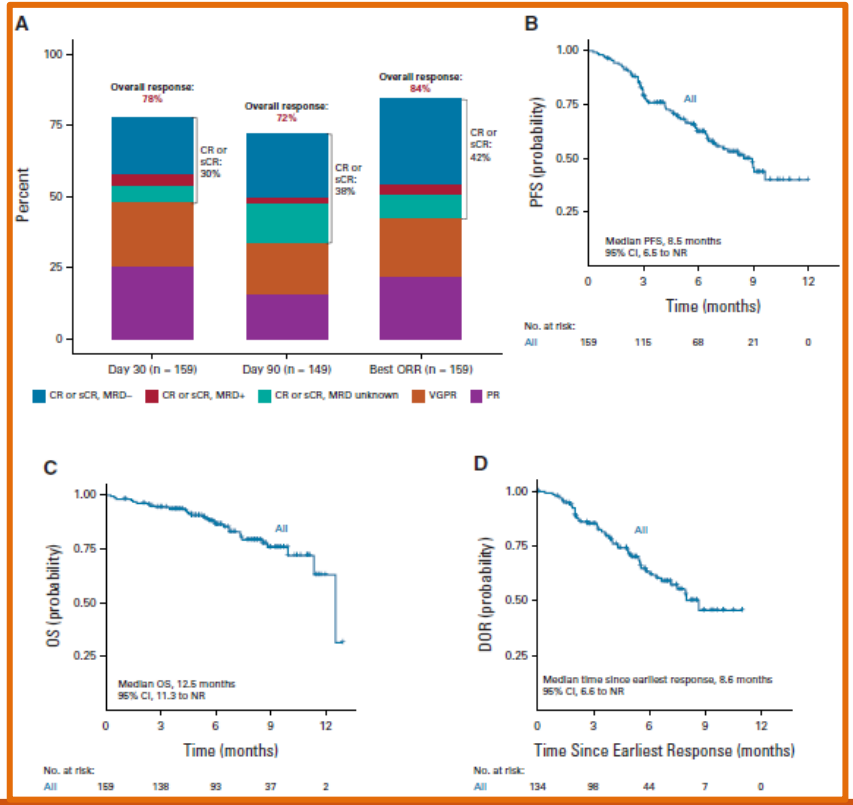


Munshi et al, N Engl J Med 2021;384:705-16.

Idecabtagene Vicleucel for Relapsed/Refractory Multiple Myeloma: Real-World Experience From the Myeloma CAR T Consortium

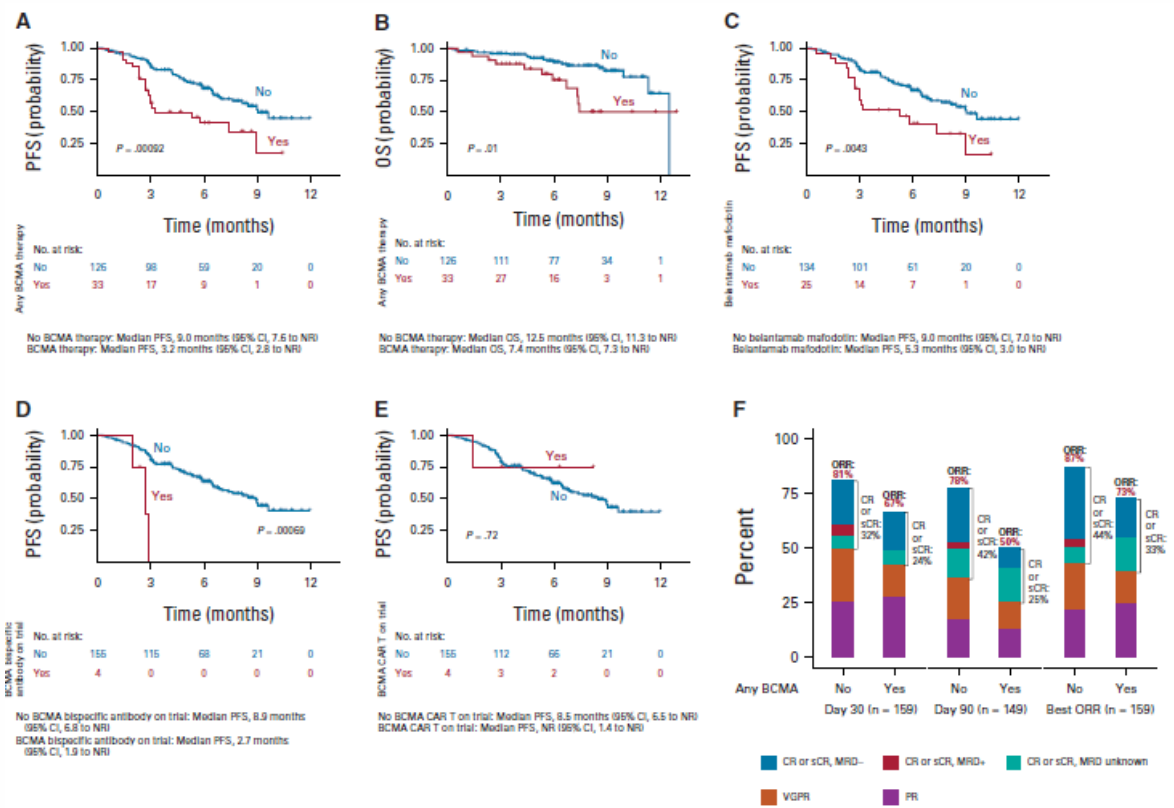
The patient population (196 pts) differed from the pivotal KarMMa clinical trial as 75% of apheresed patients would not have met trial eligibility criteria

	Best CR or Better			Best ORR			PFS		
Characteristic	N (event N)	OR (95% CI)	P	N (event N)	OR (95% CI)	P	N (event N)	HR (95% CI)	P
Prior BCMA-TT			.2			.2			**.003**
No	104 (47)	1.00 (referent)		104 (94)	1.00 (referent)		104 (42)	1.00 (referent)	
Yes	31 (10)	0.48 (0.17 to 1.29)		31 (23)	0.46 (0.13 to 1.75)		31 (18)	2.81 (1.44 to 5.51)	
High-risk cytogenetics			.4			.1			
No	86 (38)	1.00 (referent)		86 (77)	1.00 (referent)		86 (33)	1.00 (referent)	**.003**
Yes	49 (19)	0.74 (0.35 to 1.53)		49 (40)	0.43 (0.13 to 1.33)		49 (27)	2.31 (1.34 to 3.97)	
Extramedullary disease			.5			.06			.06
No	70 (29)	1.00 (referent)		70 (65)	1.00 (referent)		70 (25)	1.00 (referent)	
Yes	65 (28)	1.27 (0.62 to 2.66)		65 (52)	0.30 (0.08 to 0.98)		65 (35)	1.68 (0.97 to 2.90)	
CAR T-cell dose			> .9			.3			.6
$< 400 \times 10^6$	57 (24)	1.00 (referent)		57 (46)	1.00 (referent)		57 (26)	1.00 (referent)	
$\geq 400 \times 10^6$	78 (33)	0.96 (0.47 to 2.00)		78 (71)	1.88 (0.62 to 5.91)		78 (34)	0.86 (0.50 to 1.47)	
ECOG PS at LD			.1			.4			**.02**
0-1	108 (49)	1.00 (referent)		108 (96)	1.00 (referent)		108 (42)	1.00 (referent)	
2-4	27 (8)	0.44 (0.16 to 1.12)		27 (21)	0.55 (0.15 to 2.13)		27 (18)	2.19 (1.16 to 4.14)	
Penta-refractory			.4			.1			.8
No	76 (31)	1.00 (referent)		76 (70)	1.00 (referent)		76 (33)	1.00 (referent)	
Yes	59 (26)	1.38 (0.67 to 2.88)		59 (47)	0.41 (0.12 to 1.30)		59 (27)	0.92 (0.53 to 1.58)	
Patient age	135 (57)	1.00 (0.96 to 1.04)	> .9	135 (117)	0.87 (0.91 to 1.03)	.4	135 (60)	0.97 (0.95 to 1.00)	**.04**
Prior lines of therapy	135 (57)	1.02 (0.89 to 1.18)	.7	135 (117)	0.99 (0.82 to 1.19)	.9	135 (60)	0.97 (0.88 to 1.07)	.5



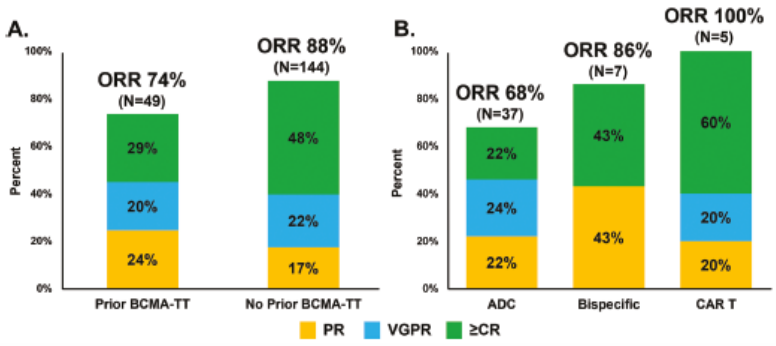
Hansen DK et al, JCO 2023; 41: 2087

PFS and OS estimated by prior anti-BCMA exposure

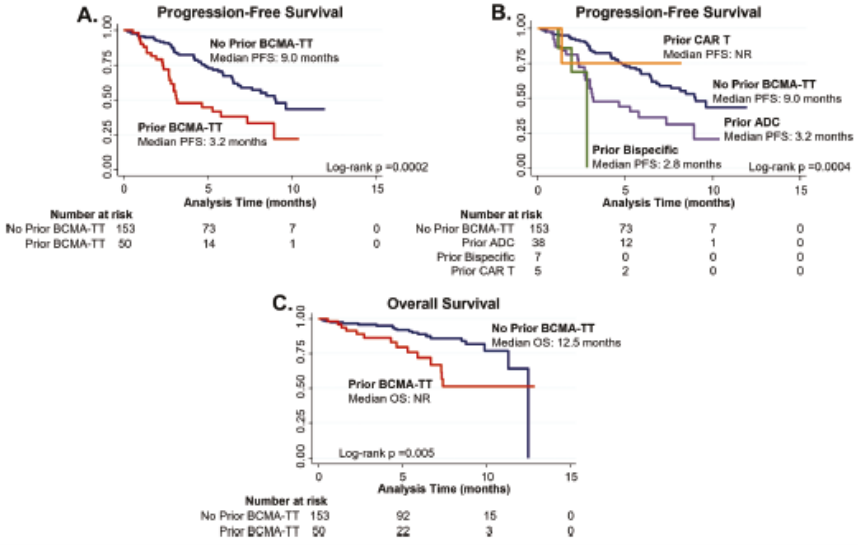


Hansen DK et al, JCO 2023; 41: 2087

Real-world experience of patients with multiple myeloma receiving ide-cel after a prior BCMA-targeted therapy



Response rates to ide-cel



Progression-free survival and overall survival

Variable	Responders (*N* = 36)	Non-responders (*N* = 13)	*P*
Duration of therapy with prior BCMA-TT in days, median (range)[a]	23 (1–208)	63 (1–370)	0.025
Time from last BCMA-TT to apheresis in days, median (range)	169.5 (30–1066)	84 (1–286)	0.017
Time from last BCMA-TT to ide-cel infusion in days, median (range)	209 (16–1118)	128 (32–362)	0.052
Ide-cel cell dose ($\times 10^6$), mean (SD)	392.3 (58.9)	397.7 (43.7)	0.95
Received systemic therapy between last BCMA-TT and apheresis, *n* (%)	28 (78%)	9 (69%)	0.539

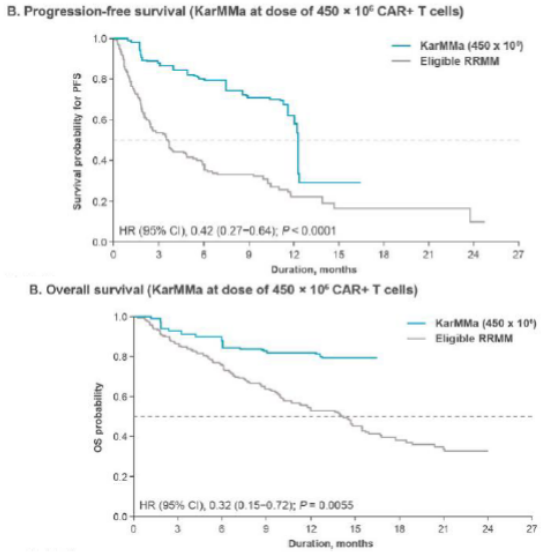
Ferreri et al, Blood Cancer Journal (2023) 13:117

Blood Cancer Journal www.nature.com/bcj

ARTICLE OPEN

KarMMa-RW: comparison of idecabtagene vicleucel with real-world outcomes in relapsed and refractory multiple myeloma

Sundar Jagannath[1,12], Yi Lin[2], Hartmut Goldschmidt[3], Donna Reece[4], Ajay Nooka[5], Alicia Senin[6], Paula Rodriguez-Otero[7], Ray Powles[8], Kosei Matsue[9], Nina Shah[10], Larry D. Anderson Jr[11], Matthew Streetly[13], Kimberly Wilson[13], Hoa Van Le[13], Arlene S. Swem[13], Amit Agarwal[13] and David S. Siegel[14]



Comparison of clinical outcomes from the real-world RRMM patients treated with currently available therapies and the patients treated with ide-cel in the KarMMa study

Response rates adjusted for stabilized trimmed inverse probability treatment weighting.

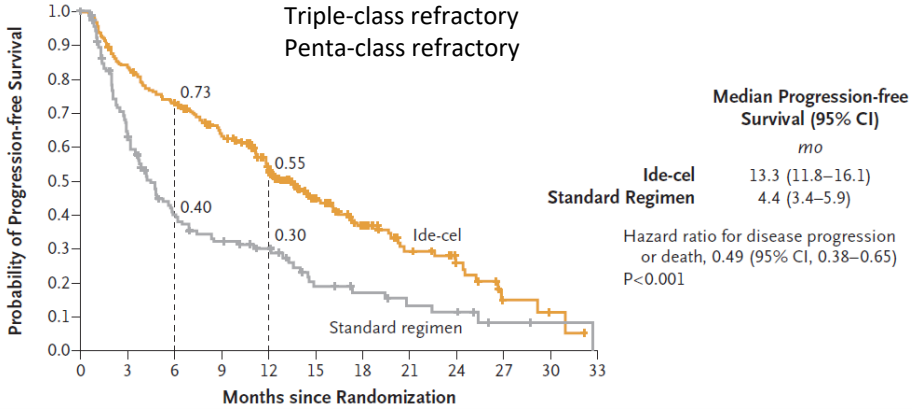
Response[a]	KarMMa cohort[b] (*N* = 128)	Eligible RRMM cohort (*N* = 190)	KarMMa cohort 450 × 10⁶ CAR + T Cells (*N* = 54)	Eligible RRMM cohort (*N* = 190)
ORR (95% CI), %	76.4 (67.8–86.1)	32.2 (24.4–42.3)	82.0 (70.3–95.7)	31.4 (25.0–39.4)
RR (95% CI)	2.4 (1.7–3.3)		2.6 (2.0–3.5)	
P	<0.0001		<0.0001	
≥VGPR[c] rate (95% CI), %	57.9 (47.8–70.1)	13.7 (8.6–21.9)	67.4 (52.6–86.4)	13.5 (9.1–20.1)
RR (95% CI)	4.2 (2.5–7.2)		5.0 (3.1–8.0)	
P	<0.0001		<0.0001	

Blood Cancer Journal 2021; 11: 116

Ide-cel or Standard Regimens in Relapsed and Refractory Multiple Myeloma

Open-label, phase 3 trial RMM, two to four regimens previously (including immunomodulatory agents, proteasome inhibitors, and daratumumab) and who had disease refractory to the last regimen, random in a 2:1 ratio to receive either ide-cel (dose range, 150×10^6 to 450×10^6 CAR-positive T cells) or one of five standard regimens.

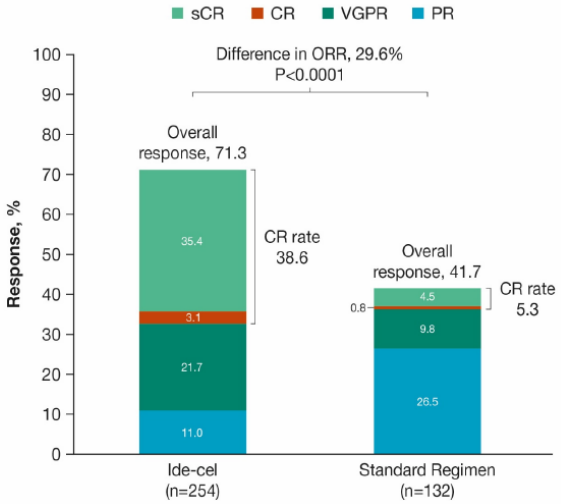
Patients were balanced for:
-HR-cytogenetics
Extramedullary disease
N° previous line
Triple-class refractory
Penta-class refractory



Median Progression-free Survival (95% CI)	*mo*
Ide-cel	13.3 (11.8–16.1)
Standard Regimen	4.4 (3.4–5.9)

Hazard ratio for disease progression or death, 0.49 (95% CI, 0.38–0.65)
P<0.001

Progression-free Survival (Intention-to-Treat Population)



Overall Response Rate (ITT Population)

KarMMa-3 ClinicalTrials.gov number, NCT03651128

Rodriguez-Otero N Engl J Med 2023; 388: 1002

Cartitude-1 study-Final results: Primary endpoint

- Single-arm, open-label phase Ib/II trial

Patients with R/R MM per IMWG and ≥3 prior regimens or double refractory to IMiD and PI and had received IMiD, PI, and anti-CD38 mAb
(N = 113)

↓

Lymphodepletion
n = 101

↓

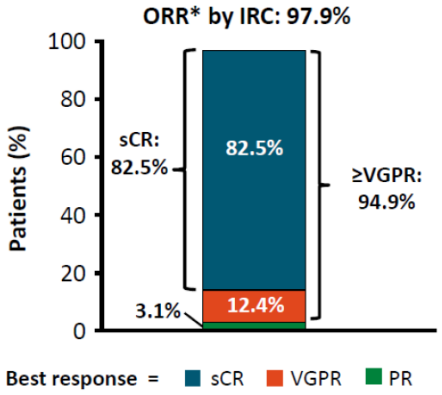
Ciltacabtagene autoleucel (n = 97)
Target 0.75 x 10^6 CAR T-cells (range 0.5-1 x 10^6)

Median administered dose:
0.71 x 10^6 (0.51 – 0.95 x 10^6) CAR+ viable T-cells/kg

Baseline characteristics:

- High-risk cytogenetics: 23.7%
- Extramedullary disease: 13.4%
- Median no. of prior therapies: 6 (range: 3-18)
- Triple refractory: 87.6%

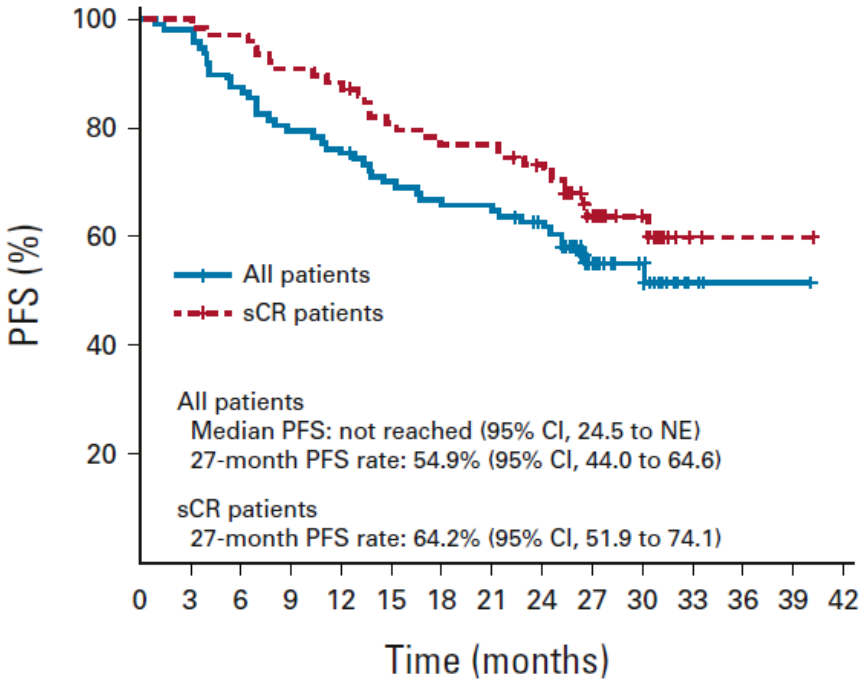
- sCR rates deepened over time
  - 67% at median 1-yr follow-up
  - 83% at median 2-yr follow-up
- Median time to first response: 1 mo (range: 0.9-10.7)
- Median time to best response: 2.6 mo (range: 0.9-17.8)
- Median time to ≥CR: 2.9 mo (range: 0.9-17.8)



J Clin Oncol 2023; 41:1265-1274.

Cartitude-1 study-Final results: Time to event outcomes

A



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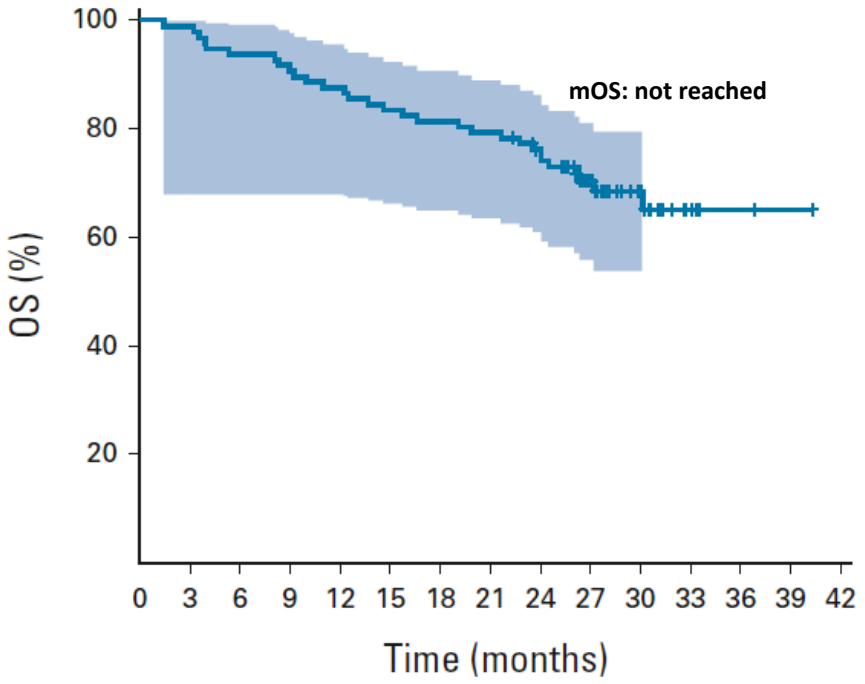

J Clin Oncol 2022; 41:1265-1274.

Clinical Drug Investigation (2022) 42:29–41
https://doi.org/10.1007/s40261-021-01100-y

ORIGINAL RESEARCH ARTICLE

Comparative Efficacy of Ciltacabtagene Autoleucel in CARTITUDE-1 vs Physician's Choice of Therapy in the Long-Term Follow-Up of POLLUX, CASTOR, and EQUULEUS Clinical Trials for the Treatment of Patients with Relapsed or Refractory Multiple Myeloma

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An external control arm for CARTITUDE-1 was created from patients in the long-term follow-up for three clinical trials of daratumumab (POLLUX, CASTOR, and EQUULEUS) who satisfied the eligibility criteria of CARTITUDE-1.

Table 3 Rates and comparative efficacy of response outcomes for cilta-cel vs physician's choice of treatment

	CARTITUDE-1	Physician's choice cohort		Unadjusted comparison		Adjusted comparison[a]	
	Observed response (%)	Observed response (%)	Adjusted[a] response (%)	OR[b] (95% CI), *p*-value	RR[b] (95% CI), *p*-value	OR[b] (95% CI), *p*-value	RR[b] (95% CI), *p*-value
ORR	97.9	37.8	33.6	78.06 (24.20, 478.16), < 0.0001	2.59 (2.26, 2.96), < 0.0001	133.01 (35.71, 887.29), < 0.0001	2.95 (2.27, 3.84), < 0.0001
≥CR rate	80.4	1.6	0.7	254.53 (105.87, 724.78), < 0.0001	50.66 (22.69, 113.09), < 0.0001	754.27 (114.19, 35258.00), < 0.0001	111.70 (29.08, 429.06), < 0.0001

Clinical Drug Investigation (2022) 42:29–41
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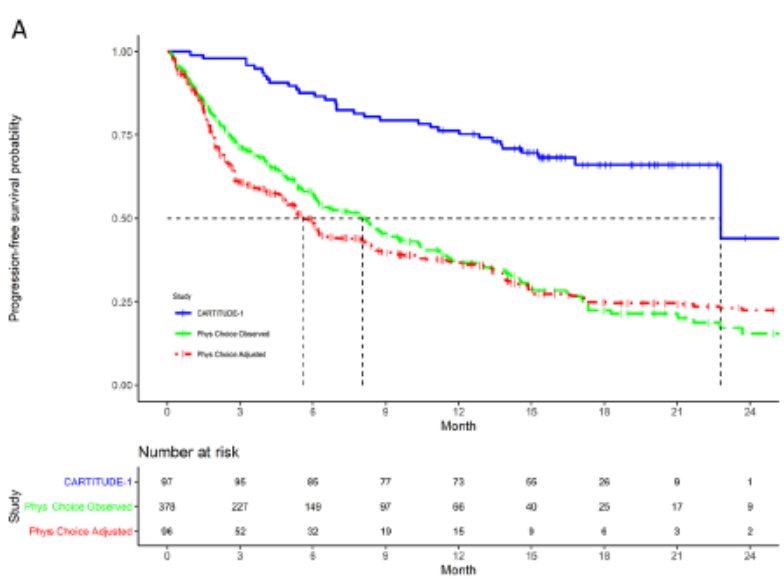
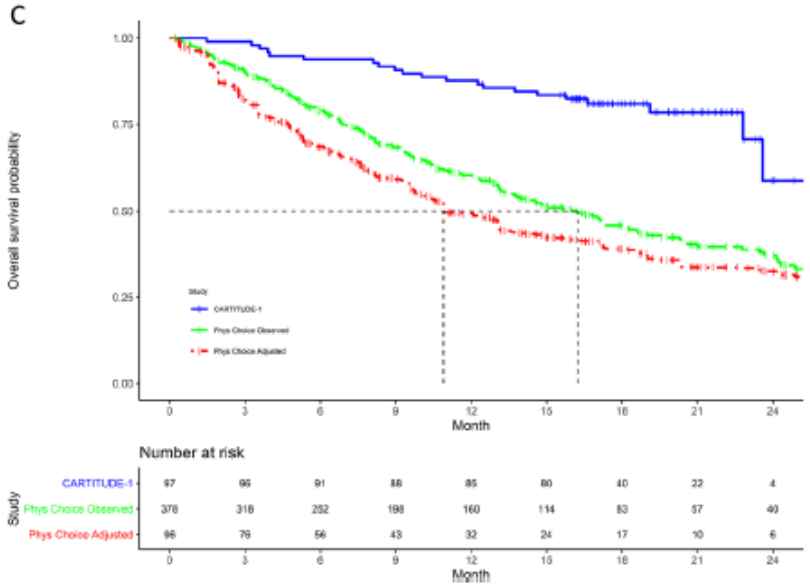
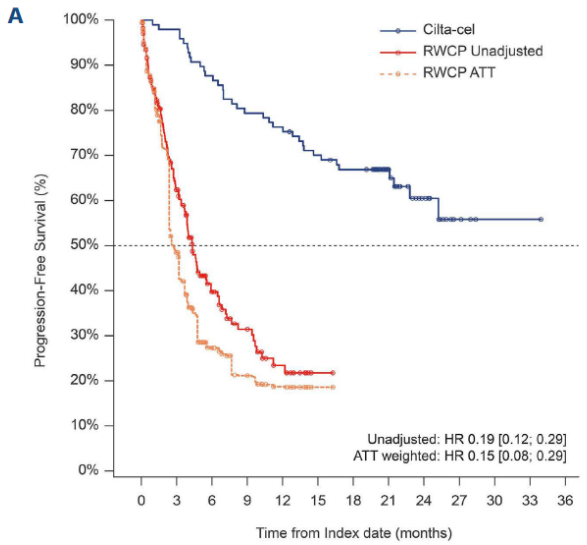
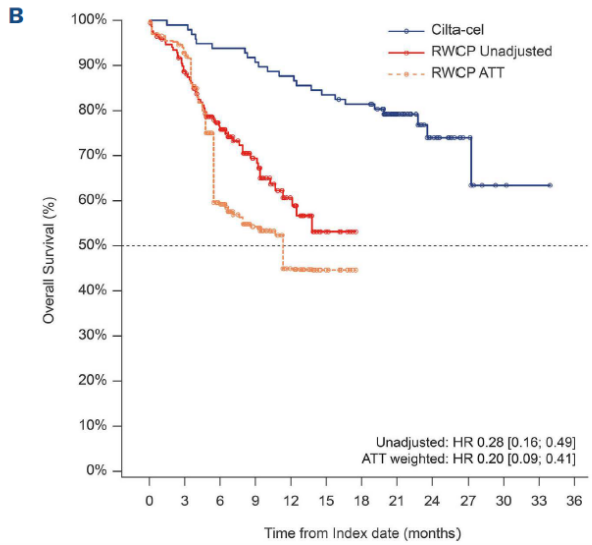




Adjusted comparison of outcomes between patients from CARTITUDE-1 versus multiple myeloma patients with prior exposure to proteasome inhibitors, immunomodulatory drugs and anti-CD38 antibody from the prospective, multinational LocoMMotion study of real-world clinical practice

Outcome	Observed response %	
	Cilta-cel (N=97)	RWCP (N=170)
ORR	97.9	42.9
≥VGPR	94.8	17.6
≥CR	82.5	0.6

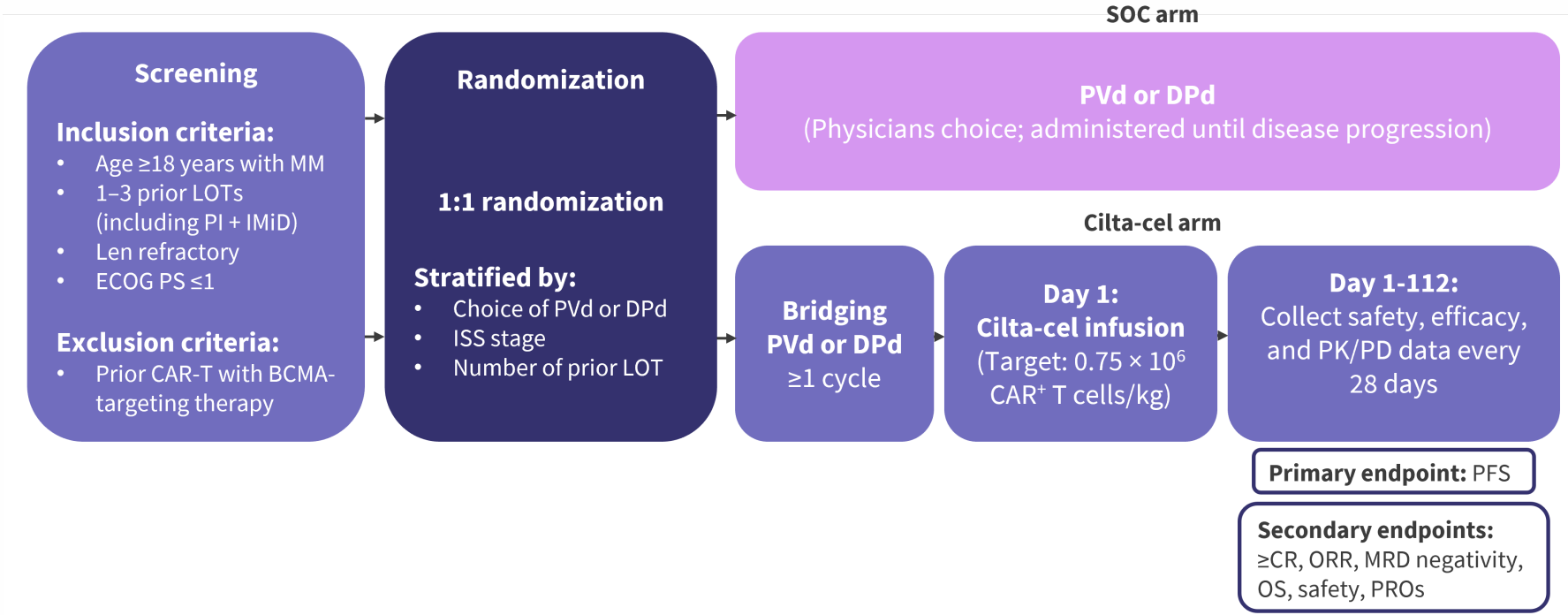




The results from this study demonstrate improved efficacy outcomes of cilta-cel versus RWCP and highlight its potential as a novel and effective treatment option for patients with multiple myeloma triple-class exposed of antimyeloma treatment.

Mateos et al, Haematologica 2023

CARTITUDE-4: Design and endpoints



San-Miguel et al, NEJM 2023

Baseline Characteristics

Characteristic	Cilta-Cel (n = 208)	SoC (n = 211)
Median age, yr (range)	61.5 (27-78)	61.0 (35-80)
Male, n (%)	116 (55.8)	124 (58.8)
White, n (%)	157 (75.5)	157 (74.4)
ECOG PS ≤1, n (%)*	207 (99.5)	210 (99.5)
ISS stage, n (%)		
▪ I	136 (65.4)	132 (62.6)
▪ II	60 (28.8)	65 (30.8)
▪ III	12 (5.8)	14 (6.6)
Bone marrow plasma cells ≥60%, n (%)	42 (20.4)	43 (20.7)
Presence of soft tissue plasmacytomas, n (%)†	44 (21.2)	35 (16.6)
Median time since diagnosis, yr (range)	3 (0.3-18.1)	3.4 (0.4-22.1)
Median prior lines of therapy, n (range)	2 (1-3)	2 (1-3)
▪ 1, n (%)	68 (32.7)	68 (32.2)
▪ 2 or 3, n (%)	140 (67.3)	143 (67.8)

Characteristic, n (%)	Cilta-Cel (n = 208)	SoC (n = 211)
Cytogenetic high risk‡	123 (59.4)	132 (62.9)
▪ del(17p)	49 (23.7)	43 (20.5)
▪ t(14;16)	3 (1.4)	7 (3.3)
▪ t(4;14)	30 (14.5)	30 (14.3)
▪ gain/amp(1q)	89 (43.0)	107 (51.0)
▪ 2+ high-risk features	43 (20.8)	49 (23.3)
▪ del(17p), t(14;16), or t(4;14)	73 (35.3)	69 (32.9)
Triple-class exposed§	53 (25.5)	55 (26.1)
Penta-drug exposed‖	14 (6.7)	10 (4.7)
Refractory status		
▪ Triple-class refractory¶	30 (14.4)	33 (15.6)
▪ Bortezomib	55 (26.4)	48 (22.7)
▪ Pomalidomide	8 (3.8)	9 (4.3)
▪ Daratumumab	48 (23.1)	45 (21.3)
▪ Any PI	103 (49.5)	96 (45.5)

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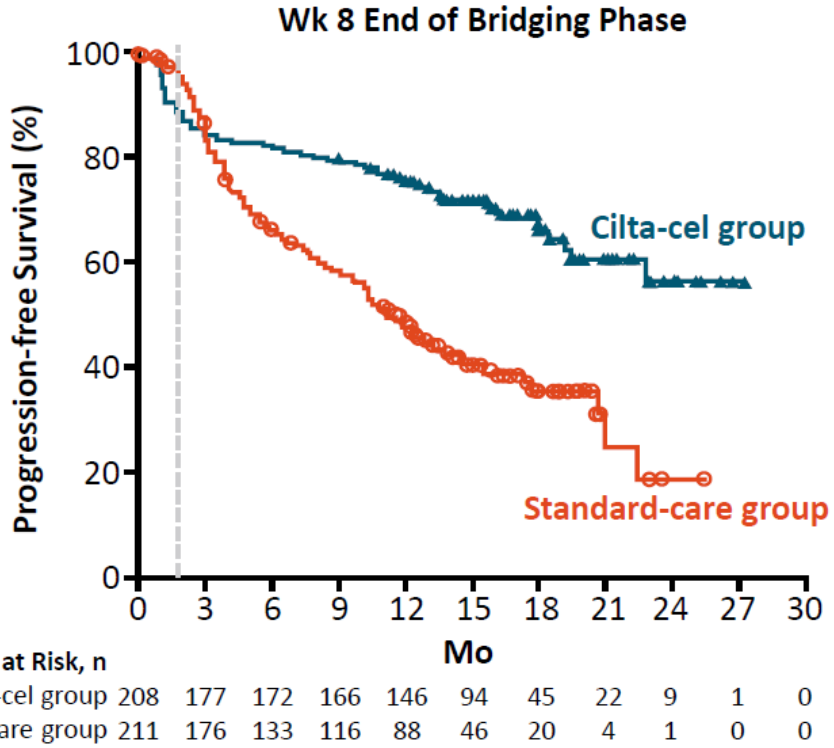
Progression-Free Survival (ITT Population)

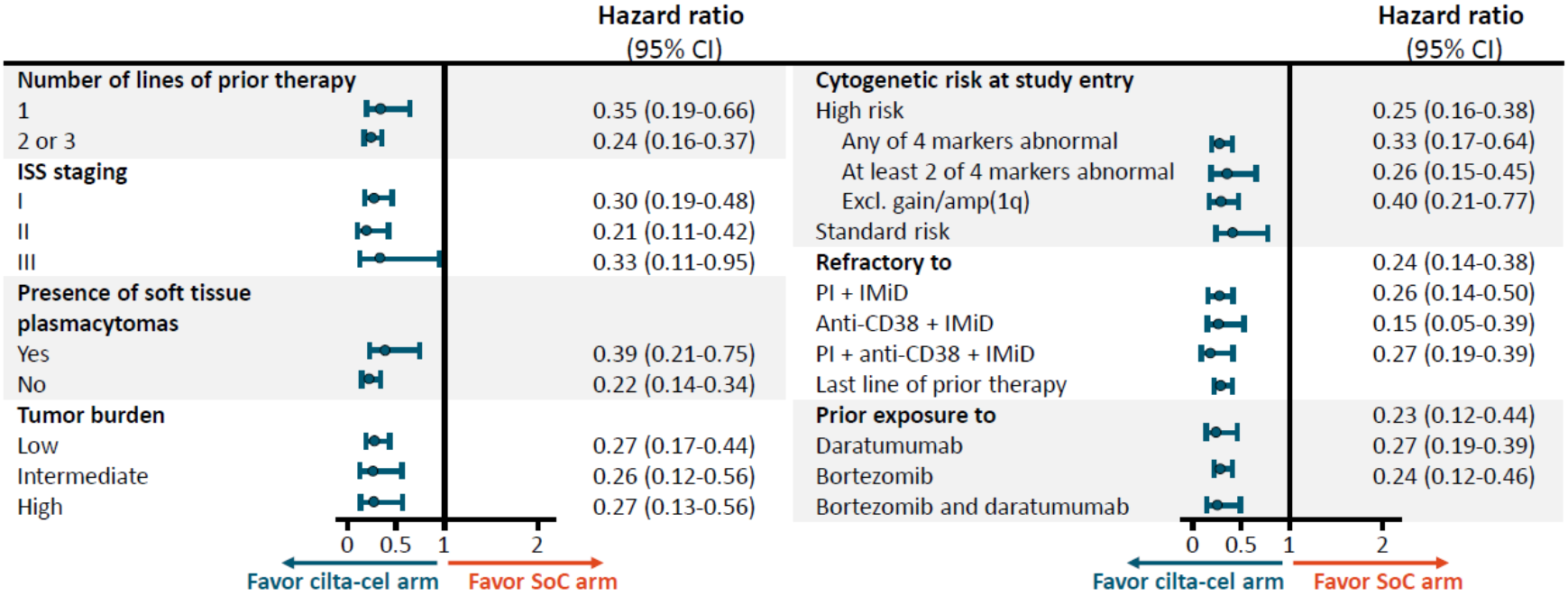


	Cilta-Cel (n = 208)	SoC (n = 211)
mPFS, mo (95% CI)	NR (22.8-NE)	11.8 (9.7-13.8)
	HR: 0.26 (95% CI: 0.18-0.38; *P* <.0001)	
12-mo PFS, %	76	49

Investigators concluded that cilta-cel has the potential to be the new standard of care for patients with lenalidomide-refractory MM after first relapse

San-Miguel et al, NEJM 2023

PFS in Key Subgroups



PFS benefit consistent across all patient subgroups, including number of prior lines of therapy, ISS stage, prior drug exposure, tumor burden, and refractory status

San-Miguel et al, NEJM 2023

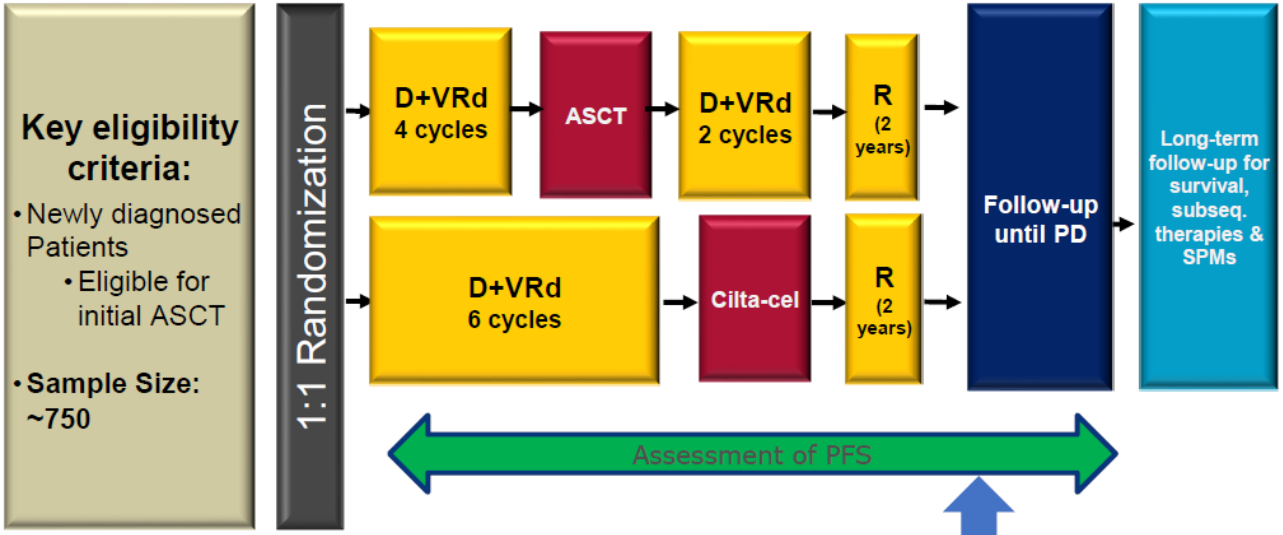
Key Secondary Endpoints (ITT)

Response Parameter	Cilta-Cel (n = 208)	SoC (n = 211)
ORR, %	84.6	67.3
▪ sCR	58.2	15.2
▪ CR	14.9	6.6
▪ VGPR	8.2	23.7
▪ PR	3.4	21.8
mDoR, mo (95% CI)	NR	16.6 (12.9-NE)
12-mo DoR, % (95% CI)	84.7 (78.1-89.4)	63.0 (54.2-70.6)
MRD negativity (ITT group), %	60.6	15.6
	OR: 8.7 (*P* <.0001)	

San-Miguel et al, NEJM 2023

CARTITUDE-6

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



Stratification factors:
a) ISS staging
b) Cytogenetics
c) Age

Dual Primary endpoints:
Sustained MRD neg CR and PFS

Estimated start date: October 2023

CAR-T cell Toxicity

CRS	Ide-cel treated (n=128)
Any grade, n (%)	107 (84)
Grade≥3	7 (5)
Median onset, days	1
Tocilizumab use, %	52
Steroid use,%	15
Neurotoxicity	**Ide-cel treated (n=128)**
Any grade, n (%)	23 (18)
Grade 3	5 (4)
Median time onset, days	2
Median duration, days	3

CRS	Ciltacel treated (n=97)
Any grade, n (%)	92 (95)
Grade≥3	5 (5)
Median onset, days	7 (5-8)
Neurotoxicity	**Cilta-cel treated (n=128)**
Any grade, n (%)	20 (21)
Grade≥3	9 (9)
ICANS (any grade), n (%)	16 (17)
Grade≥3	2 (2)
Median time onset, days (range)	8 (6-8)

blood advances

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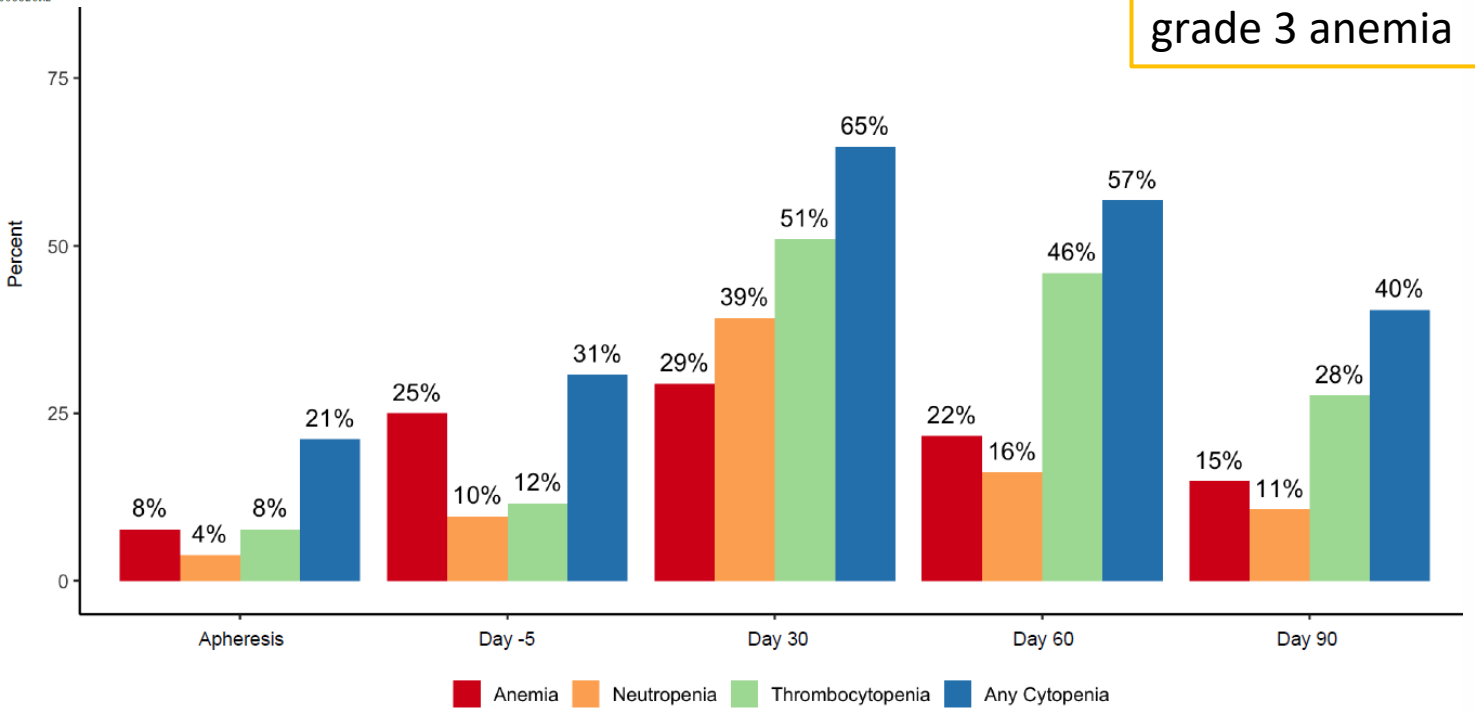
Early cytopenias and infections after standard of care idecabtagene vicleucel in relapsed or refractory multiple myeloma

Tracking no: ADV-2022-008320R2

Risk factors:
% PC pre CAR-T,
circulating PC,
grade 3 anemia



Bone marrow biopsy findings before and after ide-cel CAR-T therapy

Characteristic	Baseline (N = 52)	Day 30 (N = 48)	Day 90 (N = 37)
Marrow cellularity – n (%)			
Hypocellular	12 (23%)	19 (40%)	18 (49%)
Normocellular	19 (37%)	16 (33%)	8 (22%)
Hypercellular	21 (40%)	5 (10%)	7 (19%)
Variable	0 (0%)	5 (10%)	3 (8%)
Not evaluable	0 (0%)	3 (6%)	1 (3%)
Marrow cellularity (%) – median (range)	40 (2–99)	25 (0–75)	30 (5–95)
Not evaluable – n (%)	0 (0%)	1 (2%)	1 (3%)
% CD138$^+$ by IHC – median (range)	11.2 (0–100)	0 (0–80)	0 (0–80)
Not evaluable – n (%)	0 (0%)	2 (4%)	0 (0%)
Fibrosis grade – median (range)	0 (0–2)	0 (0–3)	0 (0–3)
Not evaluable – n (%)	0 (0%)	1 (2%)	1 (3%)
Dysplasia present – n (%)	1 (2%)	1 (2%)	0 (0%)
Not evaluable	0 (0%)	3 (6%)	1 (3%)

Supportive therapies and neutrophil recovery after ide-cel CAR-T therapy

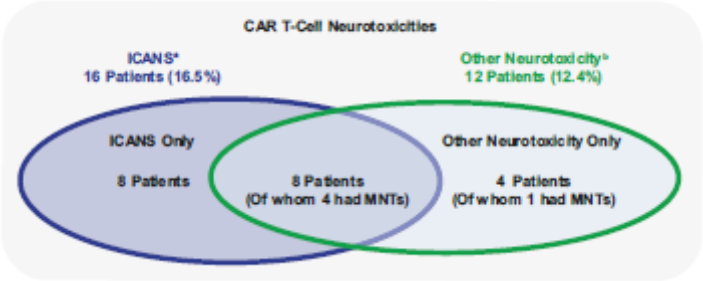
Characteristic	Value, N = 52
Granulocyte colony stimulating factor (G-CSF) – n (%)	46 (88%)
First day of G-CSF – median (range)	9 (1–93)
Last day of G-CSF – median (range)	28.5 (6–100)
CD34$^+$ stem cell boost– n (%)	4 (8%)
Day of CD34+ stem cell boost – median (range)	54 (53–76)
Dose of stem cell boost (CD34$^+$ cells × 10^6/kg) – median (range)	3.12 (1.82–7.38)
Day of neutrophil recovery – median (range)	30 (7–94)
ANC never fell below 500 cells/μL – n (%)	5 (10%)
Did not recover neutrophils prior to death, PD, or day 100 – n (%)	6 (12%)
Transfusion post-CAR T – n (%)	34 (65%)
pRBC transfusion within 7 days	27 (52%)
Platelet transfusion within 7 days	15 (29%)
pRBC transfusion > 7 days	24 (46%)
Platelet transfusion > 7 days	22 (42%)
Thrombopoietin (TPO) agonist – n (%)	11 (21%)
First day of TPO agonist – median (range)	35 (23–63)
Last day of TPO agonist – median (range)	100 (44–100)
Intravenous immunoglobulin (IVIG) – n (%)	7 (13%)
First day of IVIG – median (range)	39 (25–99)
Last day of IVIG – median (range)	100 (25–100)

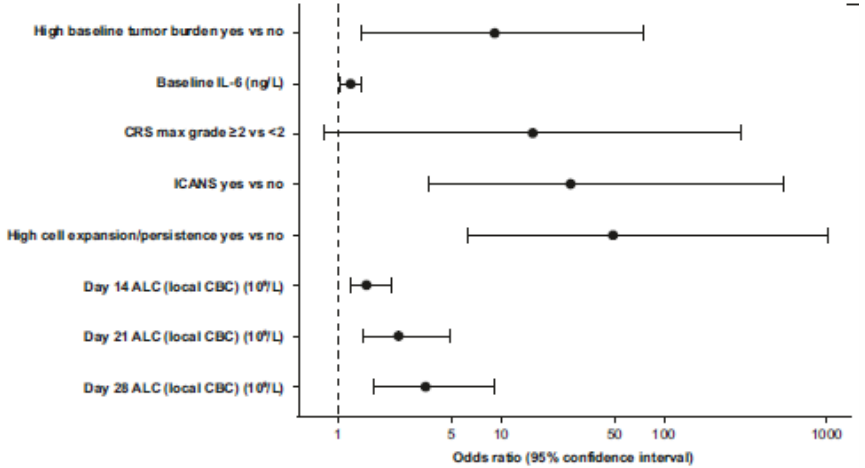
Logue JM et al, Blood Adv. 2022: 6: 6109

Incidence and management of CAR-T neurotoxicity in patients with multiple myeloma treated with ciltacabtagene autoleucel in CARTITUDE studies

Movement and neurocognitive treatment-emergent adverse events in CARTITUDE-1.

Category	Preferred term
Movement disorder	Ataxia, Balance disorder, Bradykinesia, Cogwheel rigidity, Dysgraphia, Dyskinesia, Dysmetria, Essential tremor, Gait disturbance, Hand-eye coordination impaired, Micrographia, Motor dysfunction, Myoclonus, Parkinsonism, Posture abnormal, Resting tremor, Stereotypy, Tremor
Cognitive impairment	Amnesia, Apraxia, Bradyphrenia, Cognitive disorder, Confusional state, Depressed level of consciousness, Disturbance in attention, Encephalopathy, Incoherent, Leukoencephalopathy, Loss of consciousness, Memory impairment, Mental impairment, Mental status changes, Non-infective encephalitis, Psychomotor retardation
Personality changes	Flat affect, Personality change, Reduced facial expression





Cohen et al, Blood Cancer Journal 2022;12:32

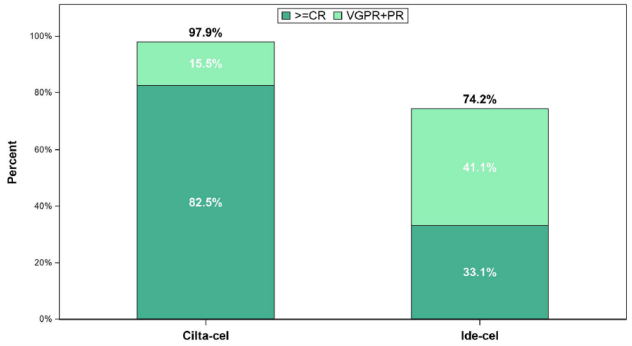
CRS and Neurotoxicity Associated With Cilta-Cel

Neurotoxicity	Cilta-Cel As-Treated Patients (n = 176)				
	Any Grade n (%)	Grade 3/4 n (%)	Median Time to Onset, Days	Median Duration, Days	Resolved, n
CRS	134 (76.1)	2 (1.1)	8	3	134
Neurotoxicity	36 (20.5)	5 (2.8)			
▪ ICANS	8 (4.5)	0	10	2	8
▪ Other	30 (17.0)	4 (2.3)			
— Cranial nerve palsy	16 (9.1)	2 (1.1)	21	77	14
— Peripheral neuropathy	5 (2.8)	1 (0.6)	63	201	3
— MNT	1 (0.6)	0	85	--	0

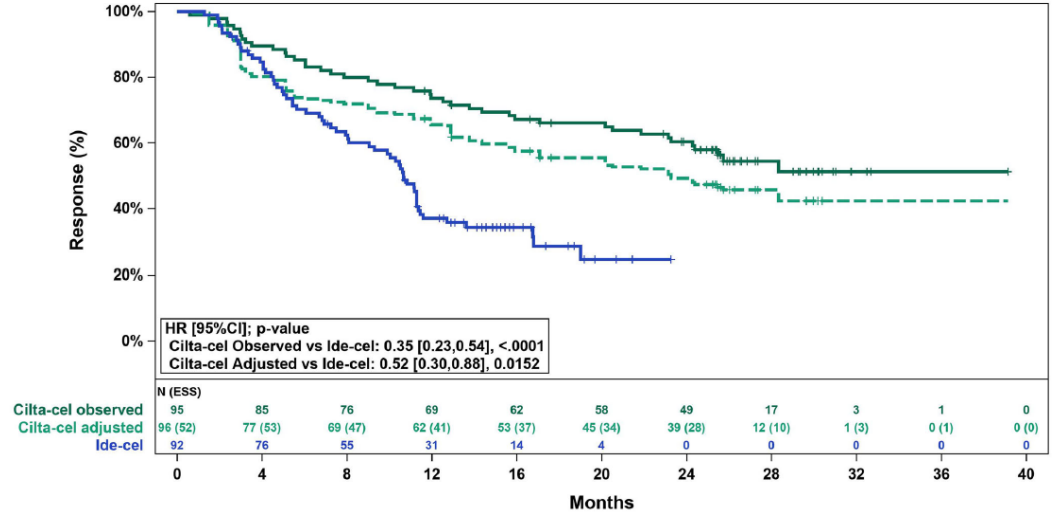
- There were no fatal neurotoxicities
- Lower incidence/severity of CRS, ICANS, MNTs, and some hematologic AEs compared with CARTITUDE-1

Cohen et al, Blood Cancer Journal 2022;12:32

Updated results from a matching-adjusted indirect comparison of efficacy outcomes for ciltacabtagene autoleucel in CARTITUDE-1 versus idecabtagene vicleucel in KarMMa for the treatment of patients with relapsed or refractory multiple myeloma



Overall response rates prior to adjustment for cilta-cel and ide-cel

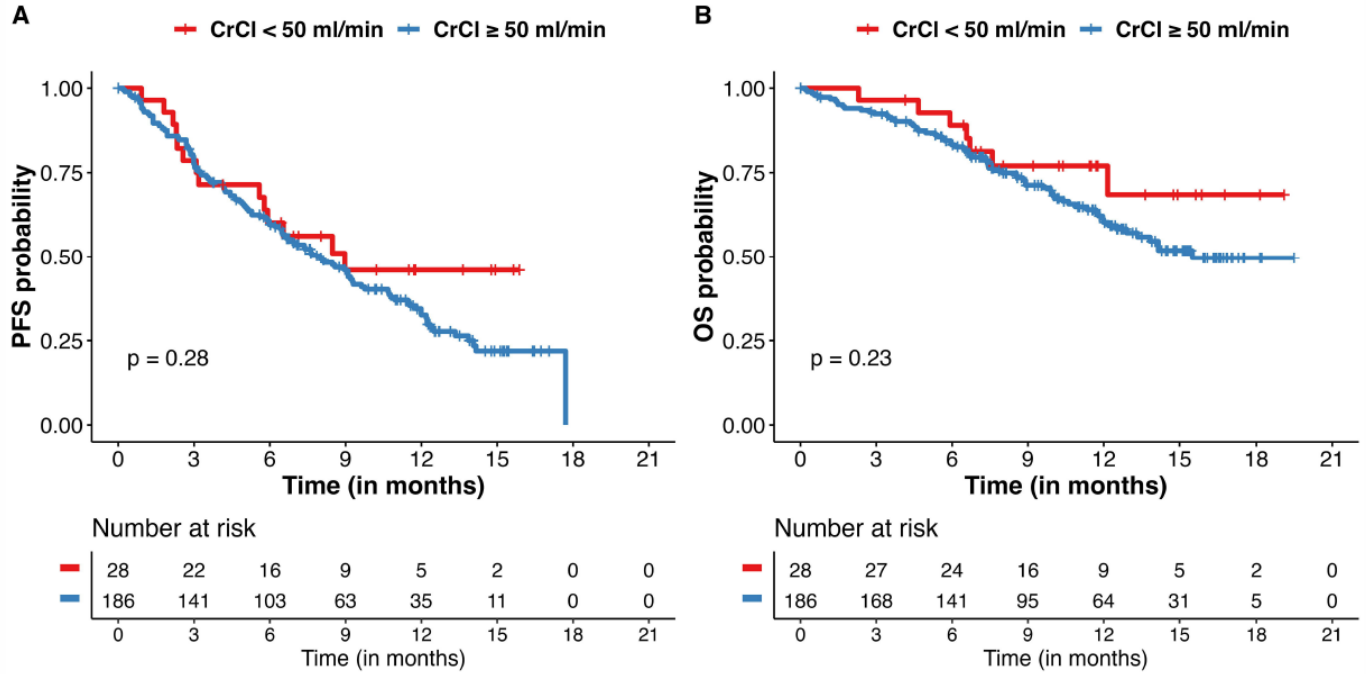


Observed (unadjusted) and adjusted (base case) Kaplan–Meier plots of progression-free survival

The results of this updated MAIC analysis using longer follow-up data showed that the superior efficacy of cilta-cel compared with ide-cel was maintained for all outcomes studied (ORR, CR rate, DoR, PFS, and OS).

CURRENT MEDICAL RESEARCH AND OPINION 2023, 39: 81–89

Idecabtagene vicleucel chimeric antigen receptor T-cell therapy for relapsed/refractory multiple myeloma with renal impairment



Patients with RI had higher incidence of short-term ≥grade 3 cytopenias, although cytopenias were similar by 3 months following CAR-T. Renal function did not worsen after CAR-T in patients with RI.

Sidana S et al, Haematologica 2023

Systematic Review

Safety and efficacy of anti-BCMA CAR-T cell therapy in older adults with multiple myeloma: A systematic review and meta-analysis

- 14 studies were included for data extraction, with a total of 558 patients, 26.2% (*n* = 146) of whom were older adults.
- The pooled ORR amongst this population was 93%, which was comparable to the ORR of 86% amongst younger patients.
- In older adults, the rates of CRS (any grade) and grade ≥ 3 were 95% and 21%, respectively. For younger patients, the pooled rate of CRS (any grade) and grade ≥ 3 CRS was 91% and 20%, respectively.
- The rate of ICANS (any grade) in older adults was 15%, which was higher than that observed in those <65 years.

Conclusion: Older adults experience comparable outcomes to younger patients with anti-BCMA CAR-T therapy, albeit with numerically higher rates of neurotoxicity.

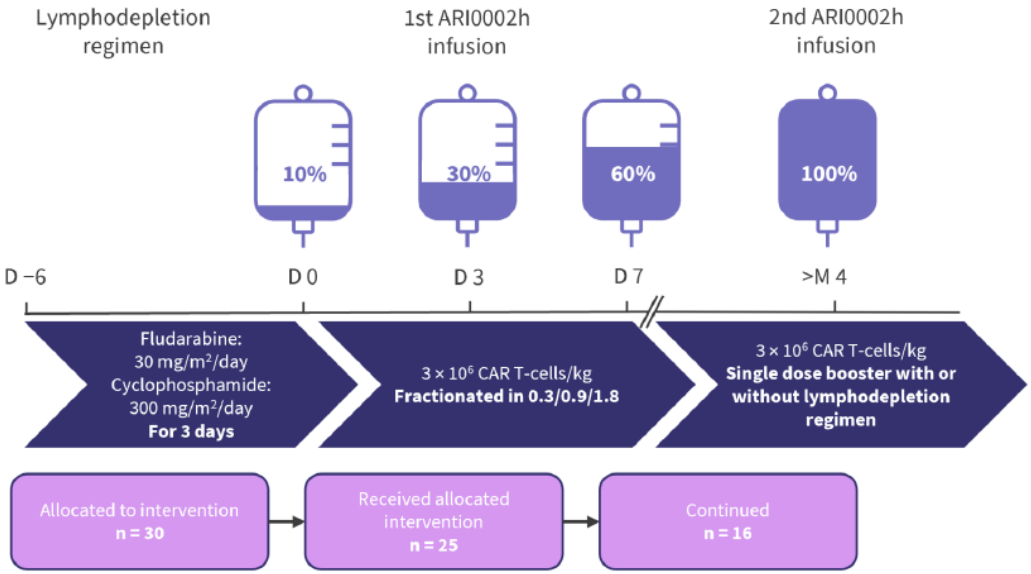
Journal of Geriatric Oncology, 2023

Fractionated initial infusion and booster dose of ARI0002h, a humanised, BCMA-directed CAR T-cell therapy, for patients with relapsed or refractory multiple myeloma (CARTBCMA-HCB-01): a single-arm, multicentre, academic pilot study

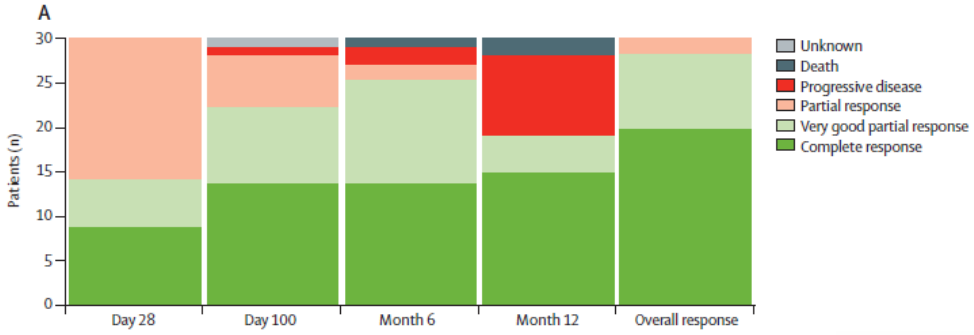
ARI0002h is a humanised 4-1BB-based BCMA-CAR T-cell therapy, lentivirally transduced on autologous T cells

35 patients, of whom 33 (94%) underwent leukapheresis and 30 (86%) received ARI0002h. The median manufacturing time of ARI0002h was 10 days .

All 30 patients received fractions 1 and 2. Five (17%) patients did not receive the third fraction of the first dose of ARI0002h because of cytokine-release syndrome. 24 (86%) of 28 eligible patients received the second administration of ARI0002h (booster dose) in a single infusion of 100% of the dose.



Oliver-Caldes et al, Lancet Oncol 2023; 24: 913-924



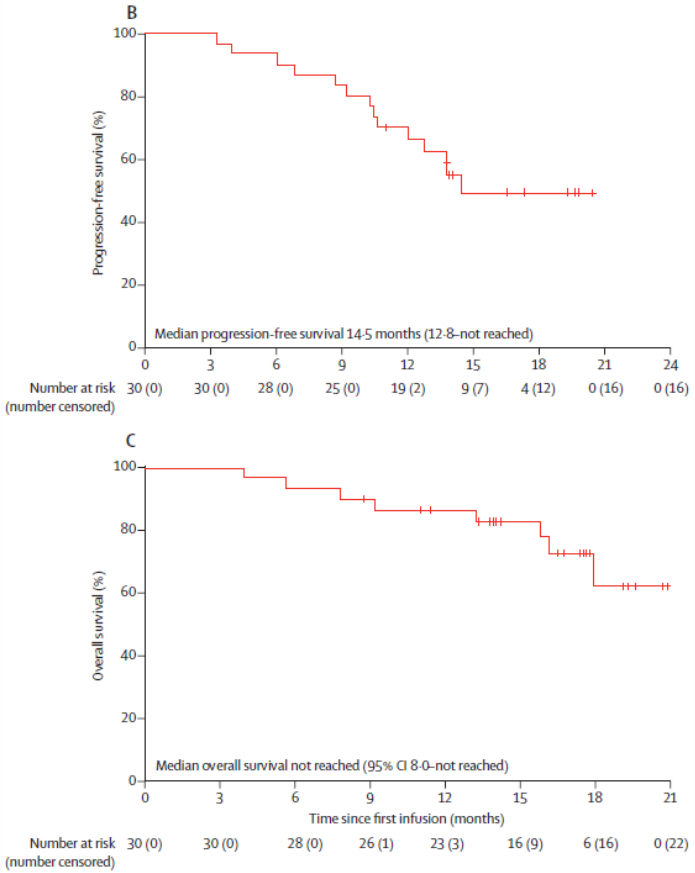
	Grade 1	Grade 2	Grade 3–4
Cytokine release syndrome	15/24 (63%)	9/24 (38%)	0
Immune effector cell-associated neurotoxicity syndrome	0	0	0
Infusion reaction	1/30 (3%)	0	0
Tumour lysis syndrome	0	1/30 (3%)	0
Persistent cytopenias	0	0	20/30 (67%)

Data are n (%). Adverse events of special interest are depicted per MedDRA preferred term.

Table 2: **Adverse events of special interest**

Prolonged cytopenias were reported in 20 (67%) of 30 patients. The median duration of grade 4 neutropenia was 35 days (95% CI 26–44) and time to complete resolution of cytopenias was 4 months (95% CI 3–5) for neutropenia, 12 months (6–18) for thrombocytopenia, and 3 months (1–13) for anaemia. All patients recovered without requiring a stem-cell boost.

ARI0002h administered in a fractioned manner with a booster dose after 3 months can provide deep and sustained responses in patients with relapsed or refractory multiple myeloma, with a low toxicity, especially in terms of neurological events, and with the possibility of a point-of-care approach



Oliver-Caldes et al, Lancet Oncol 2023; 24: 913-924

Conclusions

- CAR T-cell therapy is a promising immunotherapeutic approach in the treatment of multiple myeloma.
- The recent approval of the first two CAR T-cell products could result in improved outcomes.
- However, despite the efficacy, the significance of associated toxicities must not be underestimated.
- It is imperative for clinicians to maintain vigilance about potential AE to optimize patients selection, preemptive measures and adequate management.
- CAR-T remains a complex and expensive technology, which poses challenges to health-care systems.

Gemelli

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Grazie per l'attenzione