Convegno Interregionale SIE

Delegazione Triveneto

NUOVE TERAPIE NEI LINFOMI B AGGRESSIVI E NEL MIELOMA MULTIPLO

CRO Aviano (PN)
9 ottobre 2024

CAR-T nella terapia di salvataggio del Mieloma Multiplo
F. Patriarca (Udine)

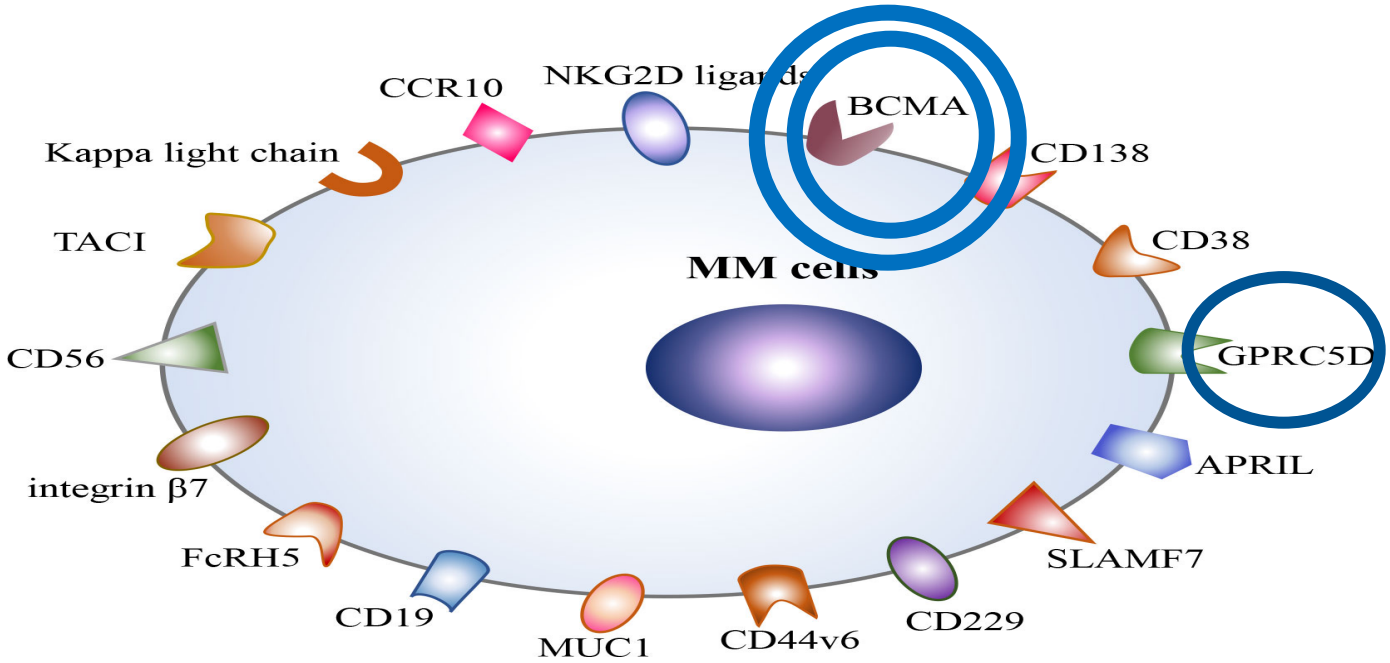
Disclosures of Francesca Patriarca

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
BMS						X	
Menarini					X		
Sanofi					x	X	
Novartis					x	X	

OUTLINE

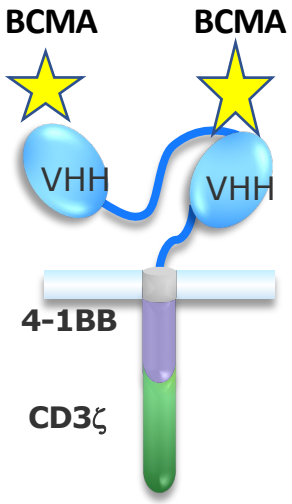
- Registrative studies and real life of ide-cel and cilta-cel
- MM specific scores
- Randomized studies
- Studies in early MM

Potential Therapeutic Targets of CAR-T cells in MM



Zhang X et al, Front Immunology 2023

Second-generation CAR-T targeting BCMA



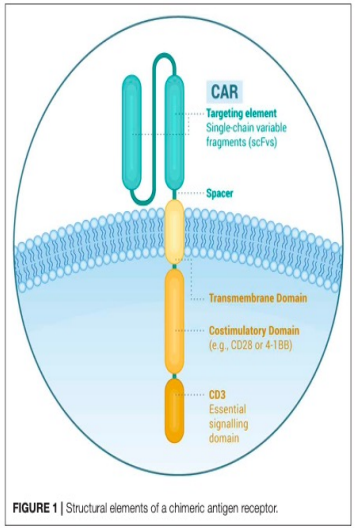


FIGURE 1 | Structural elements of a chimeric antigen receptor.

Cilta cel

Ide cel

BCMA-directed CAR-T cell product for multiple myeloma

	Ide-cabtagene vicleucel (ide-cel)	Ciltacabtagene autocel (cilta-cel)
Construct	Anti-BCMA-41BB-CD3z	Anti-BCMA2-41BB-CD3z
FDA approval status	• Adults with relapsed/refractory MM after at least 4 prior therapies, including an immunomodulating agent, a protesome inhibitor and a antiCD38-monoclonal antibody (26/3/21)	• Adults with relapsed/refractory MM after at least 4 prior therapies, including an immunomodulating agent, a protesome inhibitor and a antiCD38-monoclonal antibody (14/2/22)
EMA approval	• Adults with relapsed/refractory MM after at least 3 prior therapies, including an immunomodulating agent, a protesome inhibitor and a antiCD38-monoclonal antibody • Conditional approval 20/8/21	• Adults with relapsed/refractory MM after at least 3 prior therapies, including an immunomodulating agent, a protesome inhibitor and a antiCD38-monoclonal antibody • Conditional approval 26/5/22
AIFA approval status	• May 2024	• Pending

Clinical patients features in registrative studies

	Ide-cel	Cilta-cel
Author	Munshi et al, NEJM 2021	Berdeja et al, Lancet 2021 Martin et al, JCO 2023
Study phase	II	Ib/II
N° pts	128	97
N° previous lines	6 (3-16)	6 (3-18)
Triple class refractory	84%	88%
High risk cytogenetics	35%	24%
EMD	39%	13%
Median follow-up (months)	13	33 (1-45)

Munshi et al, NEJM 2021

Efficacy in registrative studies

	Ide-cel	Cilta-cel
Author	Munshi et al, NEJM 2021	Berdeja et al, Lancet 2021 Martin et al, JCO 2023
N° pts	128	97
OR%	73	98
CR%	33	82
Median DOR (months)	10.2	NR
Median PFS (months)	8.8	34.9

Munshi et al, NEJM 2021

ANTI-BCMA CAR-T ADVERSE EFFECTS

	Ide-cel	Cilta-cel
Study name	KarMMa	Cartitude-1
N° pts	128	97
CRS All grades ≥ Grade 3 Grade 5 **Median onset (range)**	 107 (84%) 7 (6%) 1 (> 1%) **1 (1-12)**	 92 (95%) 5 (4%) 1 (<1%) **7 (5-8)**
Neurotoxicities all grades **Grade 3-4** Grade 5	ICANS 23 (18%) **4(3%)** 4 (3%)	ICANS%parkinsonism%cranial nerve palsy 21 (21%) **11(12%)** 1 (1%)
Hematological tx Neutropenia all grades Neutropenia grade 3-4 Thrombocytopenia all grades Thrombocytopenia grade 3-4	 117 (91%) 114 (89%) 81 (63%) 67 (52%)	 93 (96%) 92 (95%) 77 (79%) 58 (60%)
Infections all grades % Infections grade 3-4 %	69% 22%	58% 20%

LATE ADVERSE EVENTS

	Ide-cel	Cilta-cel
Study name	KarMMa	Cartitude-1
N° pts	128	97
Severe adverse events	9 (7%)	6 (6%)
< 2 months	3 (CRS, lung aspergillosis, gastrointestinal hemorraghe)	2 (CRS, sepsis)
2-6 months	1 (CMV pneumonia)	3 (sepsis, lung ascess, respiratory failure)
6-24 months	5 7% SPM 1% myeloid neoplams	1 (neurotoxicity) 21% SPM 9% myeloid neoplasm 1% T-lymphoma

USA real-word experience with ide-cel

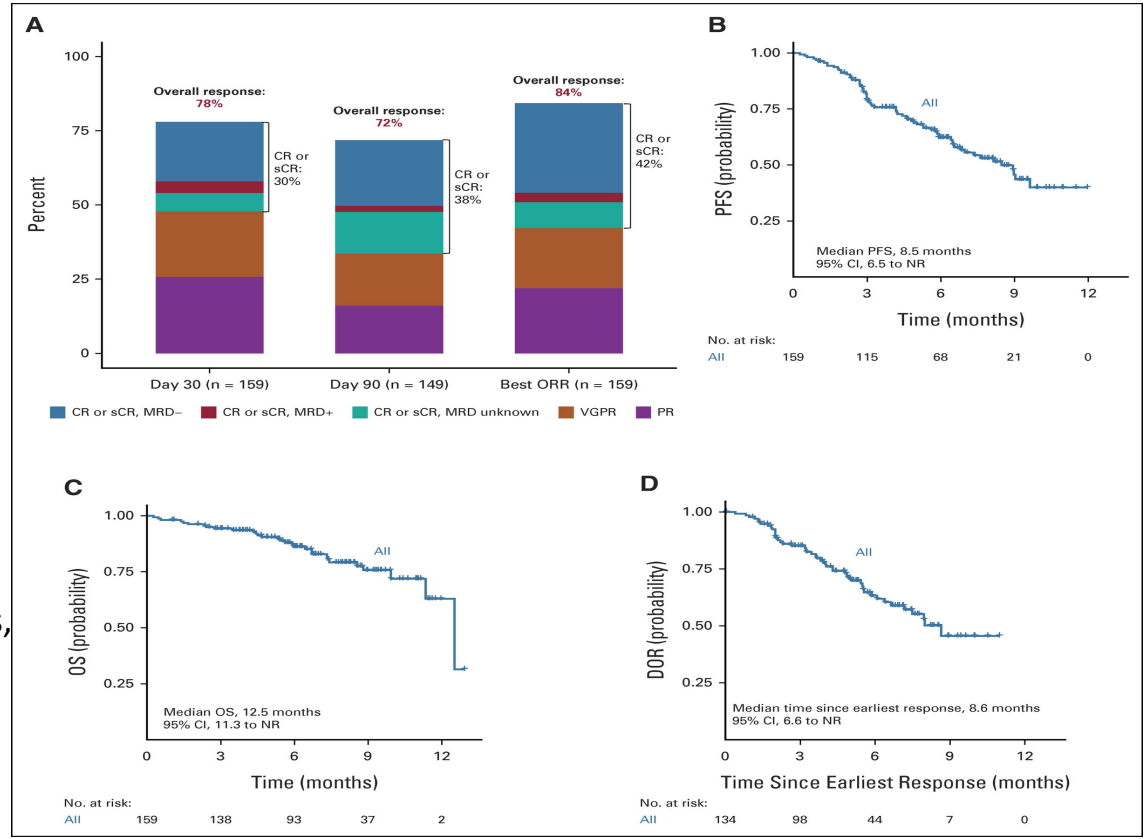
196 pts leukaphered

159 pts (81%) infused

120 pts (75%) ineligible in karMMA study due to comorbidities, organ failures, prior antiBCMA, MM complications

Similar efficacy and toxicity

Pts with previous exposure to BCMA–targeted therapy, high-risk cytogenetics, ECOG PS > 2 at lymphodepletion, and younger age had inferior PFS on multivariable analysis



Hansen D et al, JCO 2022

Outcomes in older vs. younger patients

	≥70 years (N=251), N (%)	<70 years (N=570), N (%)	*P*
Overall response	192 (76.5)	400 (70.2)	0.05
CR or better	68 (27.1)	136 (23.9)	0.29
Relapse at 6 months, %, (95% CI)	26.6 (21.0–32.7)	36.9 (32.8–41.1)	<0.01
TRM at 6 months, %, (95% CI)	5.1 (2.6–8.5)	2.7 (1.5–4.2)	0.07
PFS at 6 months, %, (95% CI)	68.3 (61.9–74.3)	60.4 (56.2–64.6)	0.03
OS at 6 months, %, (95% CI)	85.5 (80.5–89.9)	82.6 (79.2–85.7)	0.18
CRS any grade	197 (78.5)	460 (80.7)	0.46
CRS, grade ≥3	8 (3.2)	16 (2.8)	0.87
NT, any grade	93 (37.1)	138 (24.2)	<0.01
NT, grade ≥3	14 (5.6)	25 (4.4)	0.69

A p-value of <0.05 was considered statistically significant.

CR, complete response; CRS, cytokine-release syndrome; NT, neurotoxicity; OS, overall survival; PFS, progression-free survival; TRM, treatment-related mortality.

Akhtar et al on behalf of CIBMTR

Characteristics and outcomes of frail patients receiving ide-cel

Characteristic	Frail (N=343) N (%)	Non-frail (N=423) N (%)	*P*
Median age, years (range)	67.1 (29.3–85.9)	64.4 (35.0–79.7)	<0.01
ECOG PS ≥2	42 (12.2)	0 (0.0)	<0.01
Clinically significant comorbidity	334 (97.4)	253 (59.8)	<0.01
Extramedullary disease	28 (8.2)	50 (11.8)	<0.01
Relapse at 6 months, %, (95% CI)	33.9 (28.7–39.3)	33.8 (29.1–38.7)	0.65
TRM at 6 months, %, (95% CI)	5.3 (3.0–8.1)	1.9 (0.7–3.5)	0.40
PFS at 6 months, %, (95% CI)	60.9 (55.3–66.3)	64.3 (59.4–69.1)	0.35
OS at 6 months, %, (95% CI)	79.5 (74.8–83.8)	85.6 (81.9–88.9)	0.08
CRS, grade ≥3	14 (4.1)	9 (2.1)	0.06
NT, grade ≥3	21 (6.1)	17 (4.0)	0.41
Clinically significant infections	170 (49.6)	173 (40.9)	0.02
Prolonged cytopenia	67 (26.7)	161 (28.2)	0.01

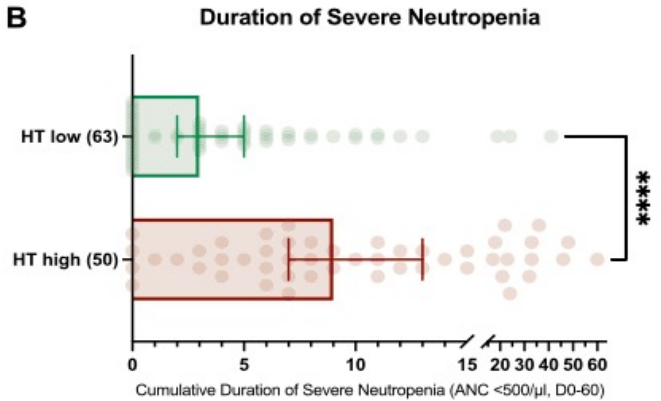
CRS, cytokine-release syndrome; ECOG, Eastern Cooperative Oncology Group; ide-cel, idecabtagene vicleucel; NT, neurotoxicity; OS, overall survival; PFS, progression-free survival; PS, performance status; TRM, treatment-related mortality.

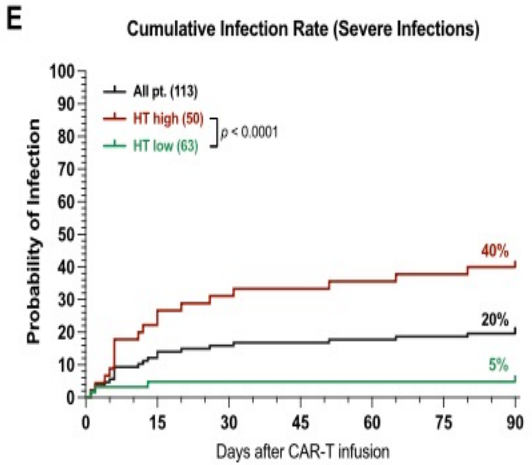
Akhtar et al on behalf of CIBMTR

SCORE HEMATOX AND OUTCOME

Retrospective study on 113 r/r multiple myeloma patients treated mainly with ide-cel across six international CAR-T centers.

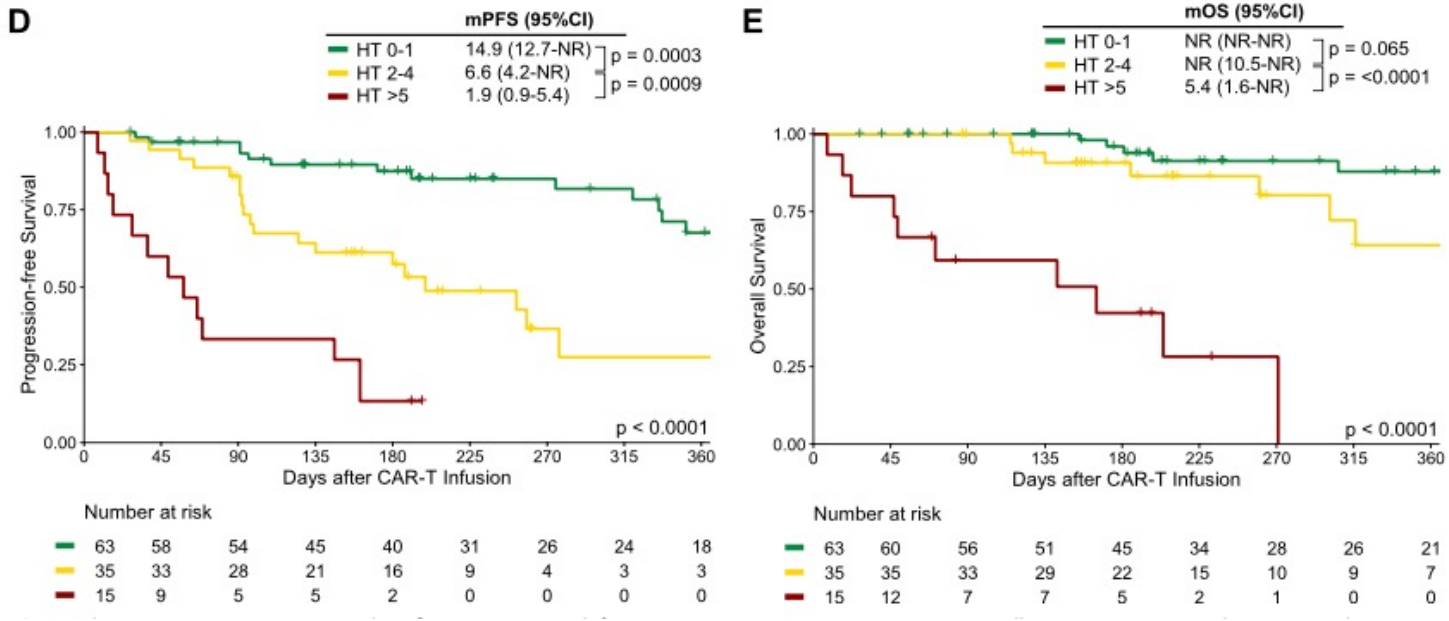
One point was allotted for the following criteria: ANC≤1200/µl, hemoglobin≤9.0 g/dl, platelet count 76–175 G/l, CRP≥3.0 mg/dl, and ferritin 650–2000 ng/ ml. Two points were provided for a platelet count≤75 G/l and ferritin ≥ 2000 ng/ml. A sum score of 2 or greater was classified as high risk (HThigh), a score of 0–1 as low risk (HTlow).UHThigh >5





Rejeski K et al, J Hematology &Oncology 2023

SCORE HEMATOX AND OUTCOME



Rejeski K et al, J Hematology &Oncology 2023

Myeloma CAR-T Relapse [MyCARe] model

International retrospective observational study including patients with RRMM infused with currently available commercial or academically produced anti–B-cell maturation antigen (BCMA) CAR-T in Europe (136) and the United States (133).

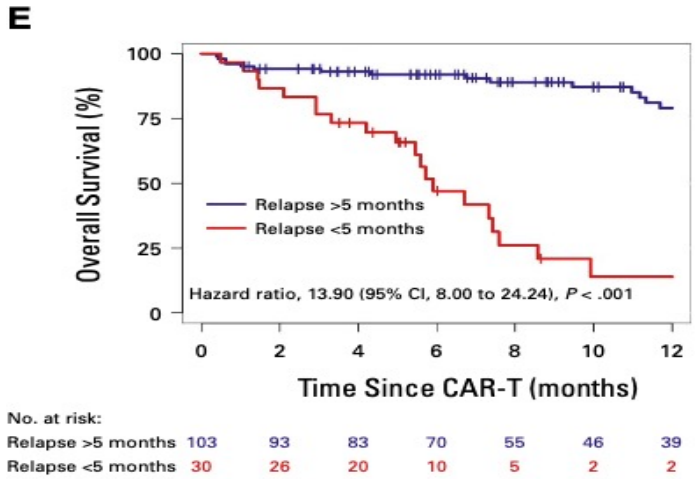
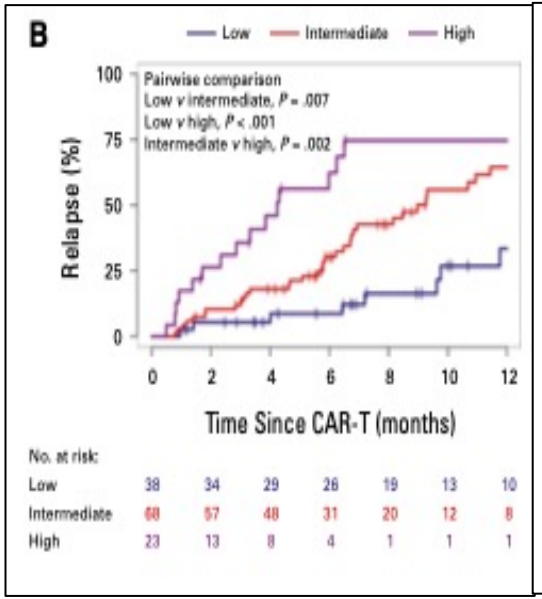


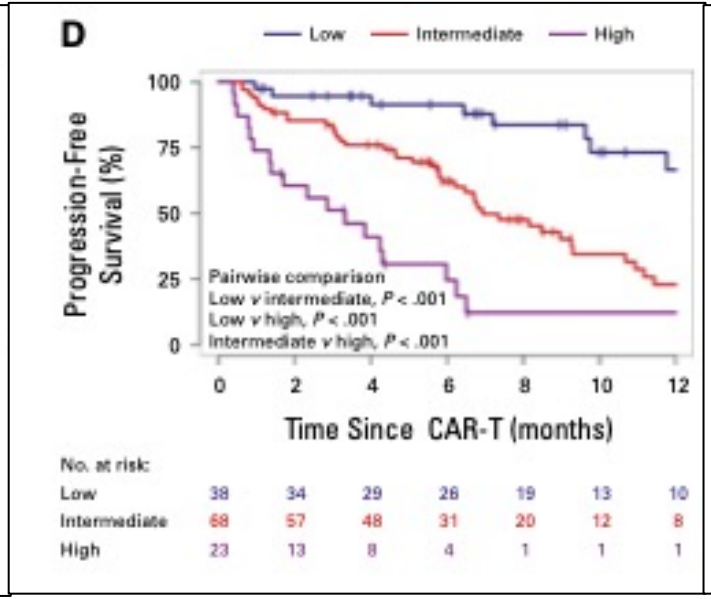
TABLE 2. Multivariable Modeling of Early Relapse/Progression

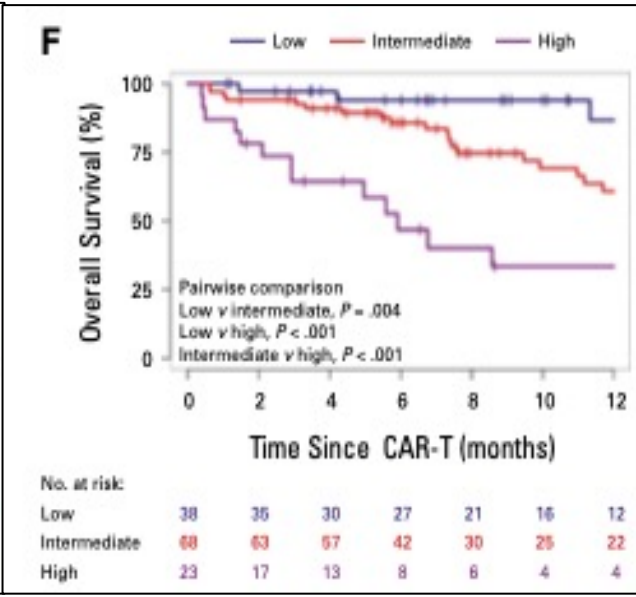
Factor	HR	95% CI	*P*	Score
EMD or PCL present	1.92	1.30 to 2.82	<.001	1
High-risk cytogenetics	1.95	1.31 to 2.92	.001	1
Ferritin > NL (sex-/age-adjusted)	1.59	1.07 to 2.37	.02	1
Lenalidomide refractoriness	1.69	1.02 to 2.82	.04	1
MyCARe risk				
Low (score 0-1)	Ref			
Intermediate (score 2-3)	3.27	1.87 to 5.72	<.001	
High (score 4)	7.89	4.21 to 14.79	<.001	

Gagelmann et al, JCO 2024

Myeloma CAR-T Relapse [MyCARe] model

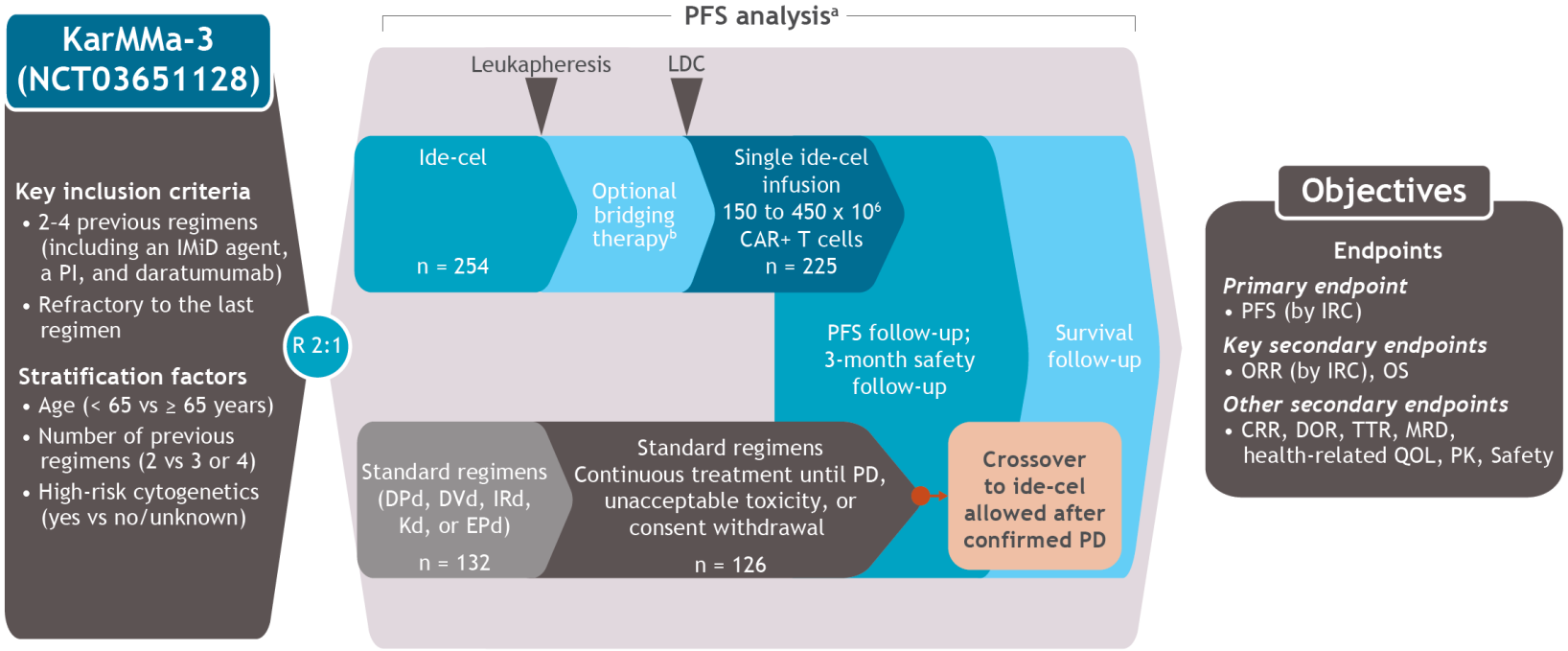






Gagelmann et al, JCO 2024

KarMMa-3 study design



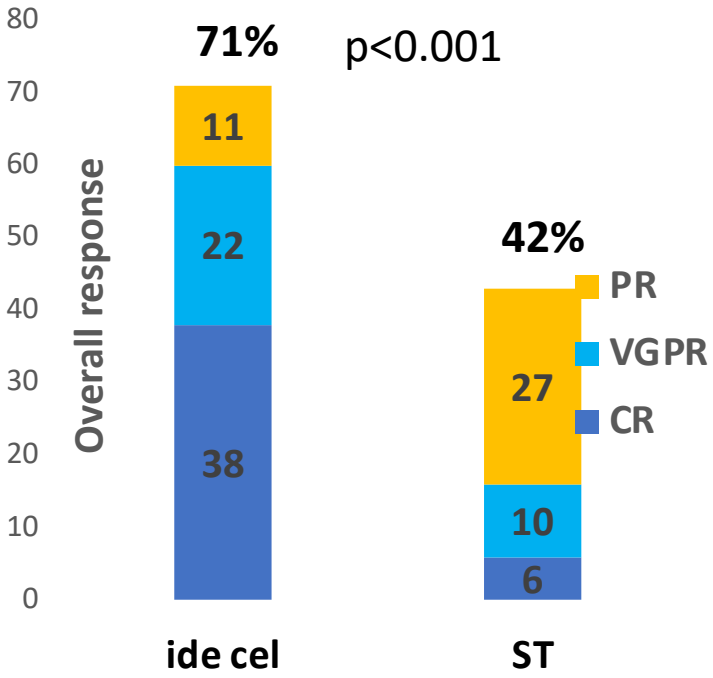
[a]Time from randomization to the first occurrence of disease progression or death from any cause according to IMWG criteria.
[b]Up to 1 cycle of DPd, DVd, IRd, Kd, or EPd may be given as bridging therapy with a minimum of 14 days of washout.
CAR, chimeric antigen receptor; CRR, complete response rate; DOR, duration of response; DPd, daratumumab/pomalidomide/dexamethasone; DVd, daratumumab/bortezomib/dexamethasone; EPd, elotuzumab/pomalidomide/dexamethasone; ide-cel, idecabtagene vicleucel; IMiD, immunomodulatory agent; IMWG, International Myeloma Working Group; IRC, independent review committee; IRd, ixazomib/lenalidomide/dexamethasone; Kd, carfilzomib/dexamethasoneLDC, lymphodepleting chemotherapy; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PI, proteosome inhibitor; PK, pharmacokinetics; QOL, quality of life; R, randomization; TTR, time to resolution.

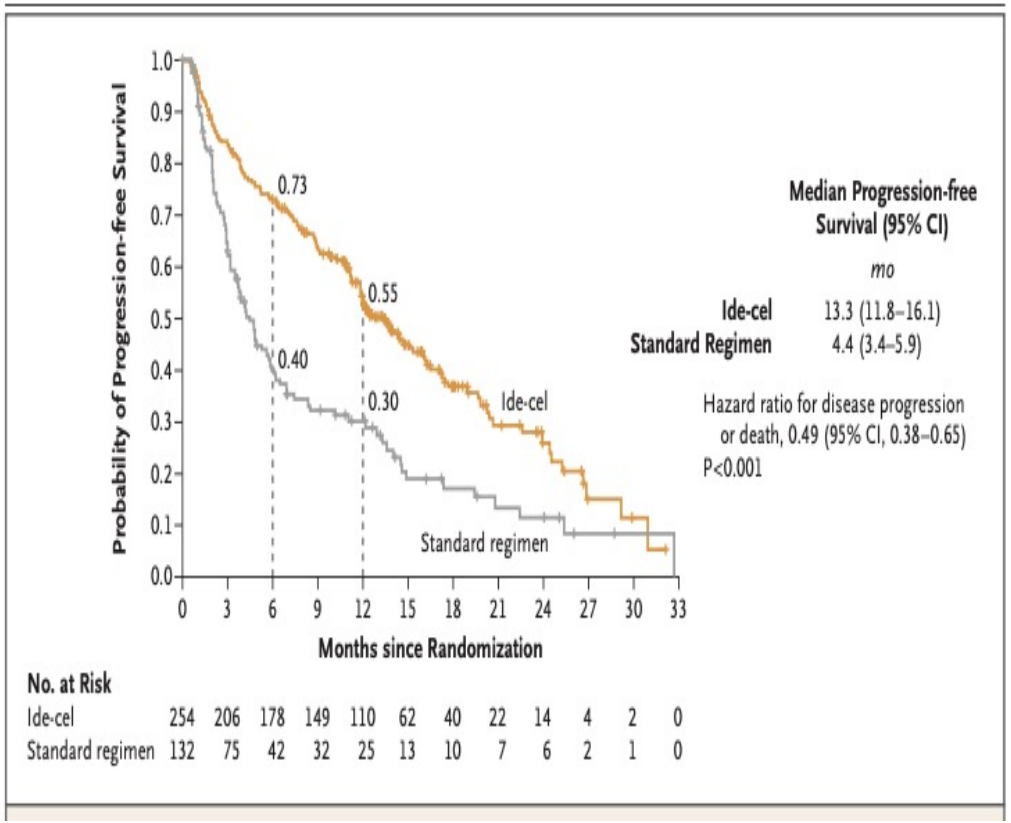
Rodriguez-Oter et al, NEJM 2023

Ide-cel or standard treatments in RR MM after 2-4 prior regimens

	Ide-cel	Standard therapy
N° pts	254	132
High risk cytogenetics	42%	46%
Extramedullary MM	24%	24%
N° previous lines	3(2-4)	3 (2-4)
Triple class refractory	65%	67%
Penta drug refractory	6%	4%

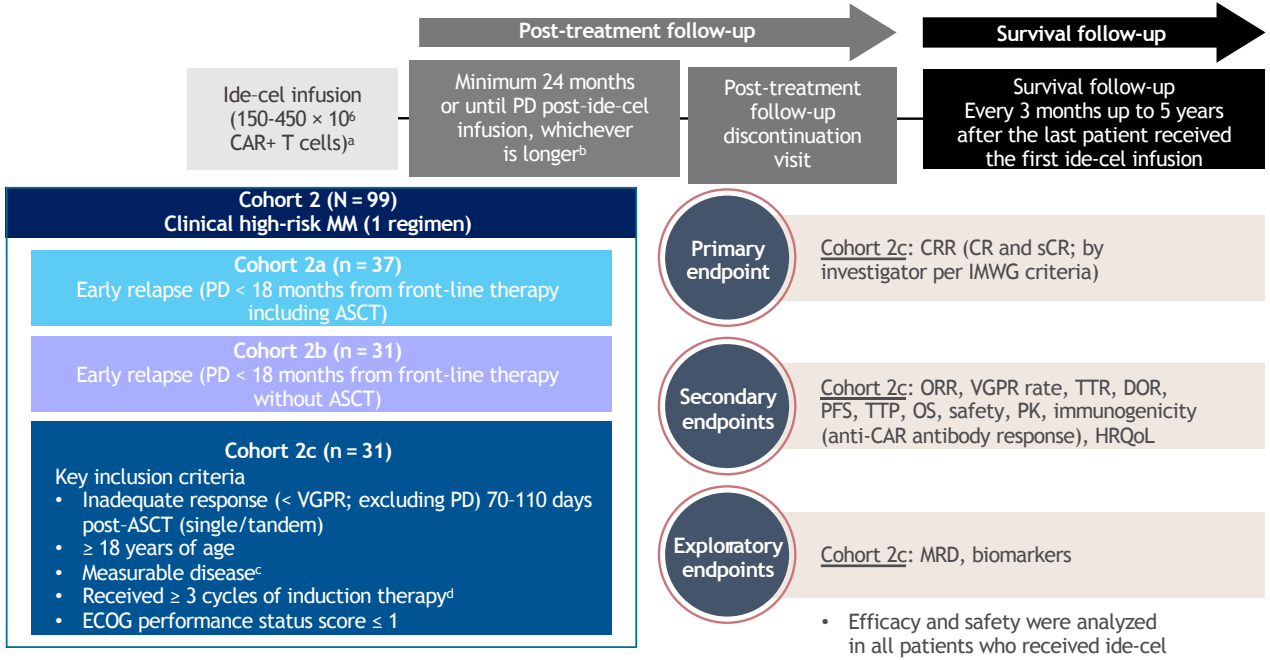
Rodriguez-Oter et al, NEJM 2023





Rodriguez-Oter et al, NEJM 2023

KarMMa-2 cohort 2 study design

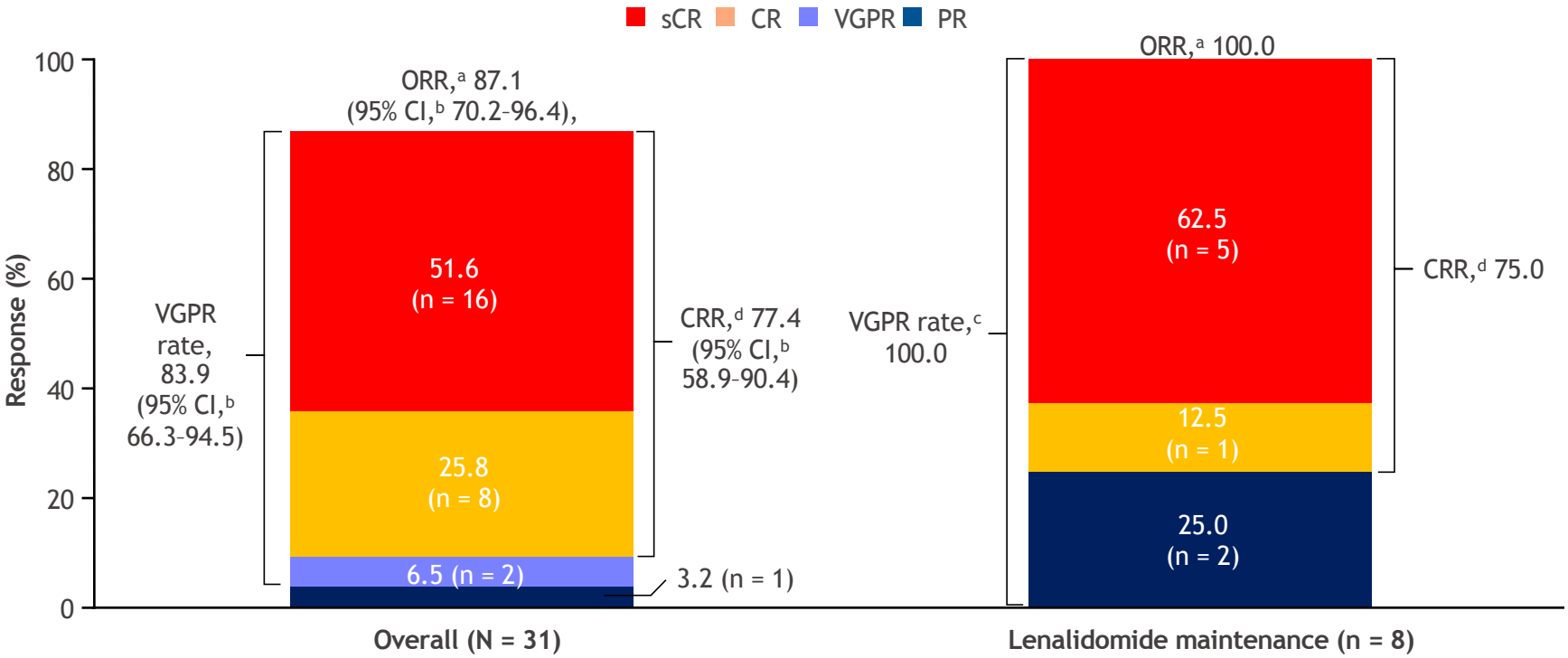


[a]After lymphodepletion (cyclophosphamide 300 mg/m² + fludarabine 30 mg/m² × 3), patients received a single infusion of ide-cel at a range of 150-450 × 10⁶ CAR+ T cells (up to an additional 20%; 20% over the protocol-specified dose constituted overdose); [b]At investigator discretion, patients could receive maintenance treatment post-infusion; [c]Measurable disease determined by M protein (serum protein electrophoresis ≥ 0.5 g/dL or urine protein electrophoresis ≥ 200 mg/24 hours) and/or light chain MM without measurable disease in serum or urine (serum immunoglobulin free light chain ≥ 10 mg/dL and abnormal serum immunoglobulin κ:λ free light chain ratio); [d]Must contain a PI, an IMiD® agent, and dexamethasone.

ASCT, autologous stem cell transplantation; CAR, chimeric antigen receptor; CR, complete response; CRR, complete response rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HRQoL, health-related quality of life; ide-cel, idecabtagene vicleucel; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; sCR, stringent complete response; TTP, time to progression; TTR, time to response; VGPR, very good partial response.

Madhav Dhodapka, abstract 2101

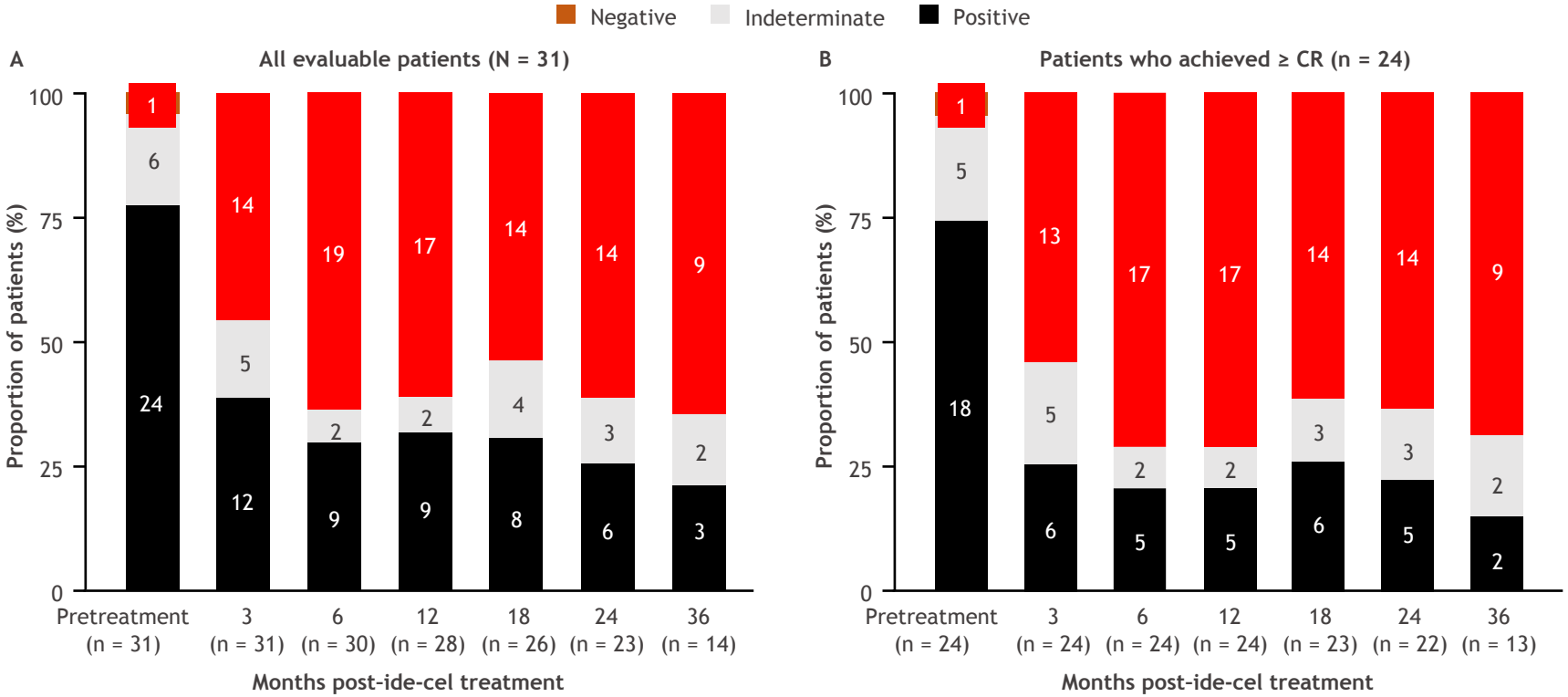
Best overall response



36-month PFS rate of 76.8%

Madhav Dhodapka, abstract 2101

MRD negativity

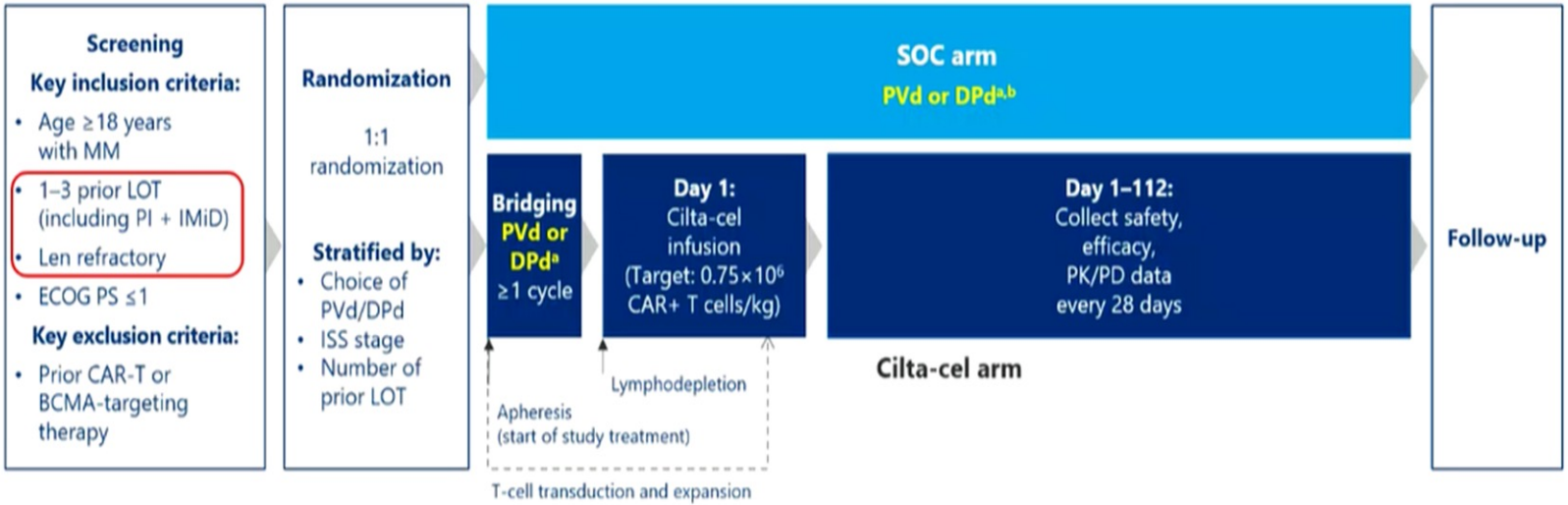


CR, complete response; ide-cel, idecabtagene vicleucel; MRD, minimal residual disease.

Madhav Dhodapka, abstract 2101

CARTITUDE-4: Study Design and Endpoints

Median follow-up was 15,4 months



Primary endpoint

- PFS[c]

Secondary endpoints

- Efficacy: ≥CR, ORR, MRD negativity, OS
- Safety
- PROs

Einsele H et al, EHA2023
San Miguel et al, NEJM 2023

[a]Physicians' choice. [b]Administered until disease progression. [c]Time from randomization to disease progression/death.
BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; CR, complete response; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; len, lenalidomide; LOT, line of therapy; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; SOC, standard of care.

CARTITUDE-4: Baseline Demographics and Disease Characteristics

Baseline characteristic	ITT population	
	Cilta-cel (n=208)	SOC (n=211)
Age, median (range), years	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 (%)[a,b]	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%,[c] n (%)	42 (20.4)	43 (20.7)
Presence of soft tissue plasmacytomas,[d] n (%)	44 (21.2)	35 (16.6)
Years since diagnosis, median (range)	3 (0.3–18.1)	3.4 (0.4–22.1)
Prior LOT, median (range)	2 (1–3)	2 (1–3)
1 prior LOT, n (%)	68 (32.7)	68 (32.2)
2 or 3 prior LOT, n (%)	140 (67.3)	143 (67.8)

Baseline characteristic	ITT population	
	Cilta-cel (n=208)	SOC (n=211)
Cytogenetic high risk, n (%)[e]	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 or more high-risk cytogenetic features	43 (20.8)	49 (23.3)
del(17p), t(14;16), or t(4;14)	73 (35.3)	69 (32.9)
Triple-class[f] exposed, n (%)	53 (25.5)	55 (26.1)
Penta-drug[g] exposed, n (%)	14 (6.7)	10 (4.7)
Refractory status, n (%)		
Triple-class refractory[f,h]	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)

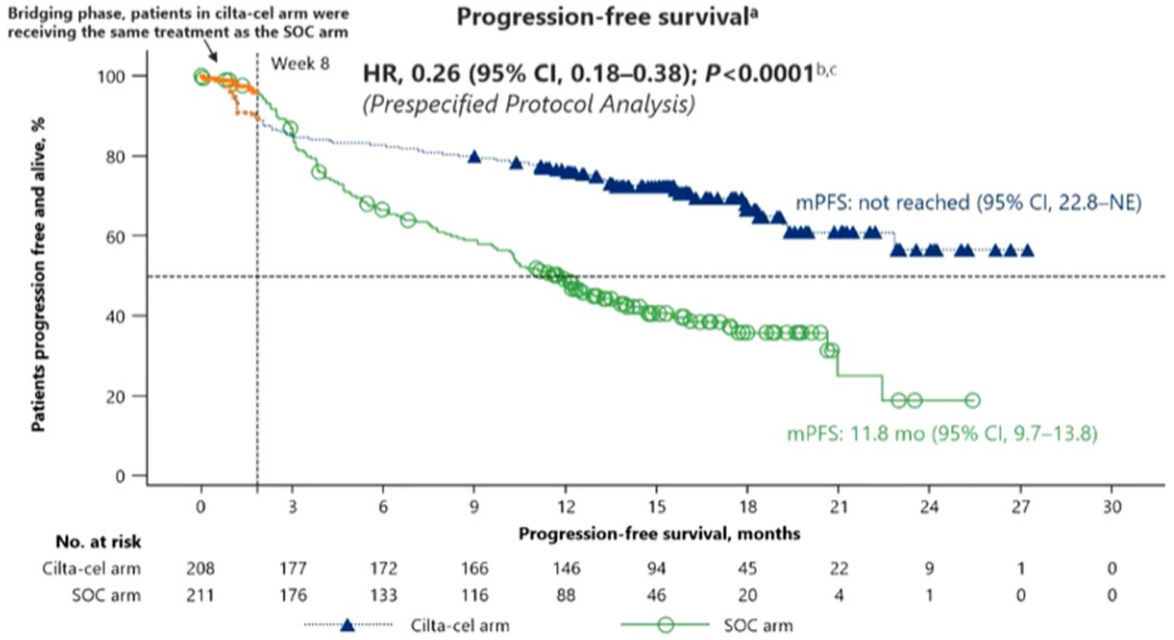
[a]1 patient in each arm had ECOG PS of 2. [b]Latest nonmissing ECOG PS score on or prior to apheresis/cycle 1 day 1 is used. [c]In 206 (cilta-cel arm) and 208 (SOC arm) patients, maximum value from bone marrow biopsy and bone marrow aspirate is selected if both results are available. [d]Including extramedullary and bone-based plasmacytomas with measurable soft tissue component. [e]In 207 (cilta-cel arm) and 210 (SOC arm) patients. [f]Including 1 PI, 1 IMiD, and 1 anti-CD38 monoclonal antibody. [g]Including ≥2 PI, ≥2 IMiDs, and 1 anti-CD38 monoclonal antibody. [h]2 patients (cilta-cel arm) and 1 patient (SOC arm) were penta-drug refractory, including ≥2 PI, ≥2 IMiDs, and 1 anti-CD38 monoclonal antibody. cilta-cel, ciltacabtagene autoleucel; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; ITT, intent-to-treat; LOT, line of therapy; PI, proteasome inhibitor; SOC, standard of care.

Einsele H et al, EHA2023, San Miguel et al N

CARTITUDE-4: Primary Endpoint – PFS (ITT Population)

Cilta-cel vs SOC

- 12-month PFS rate: 76% vs 49%
- SOC performed as expected

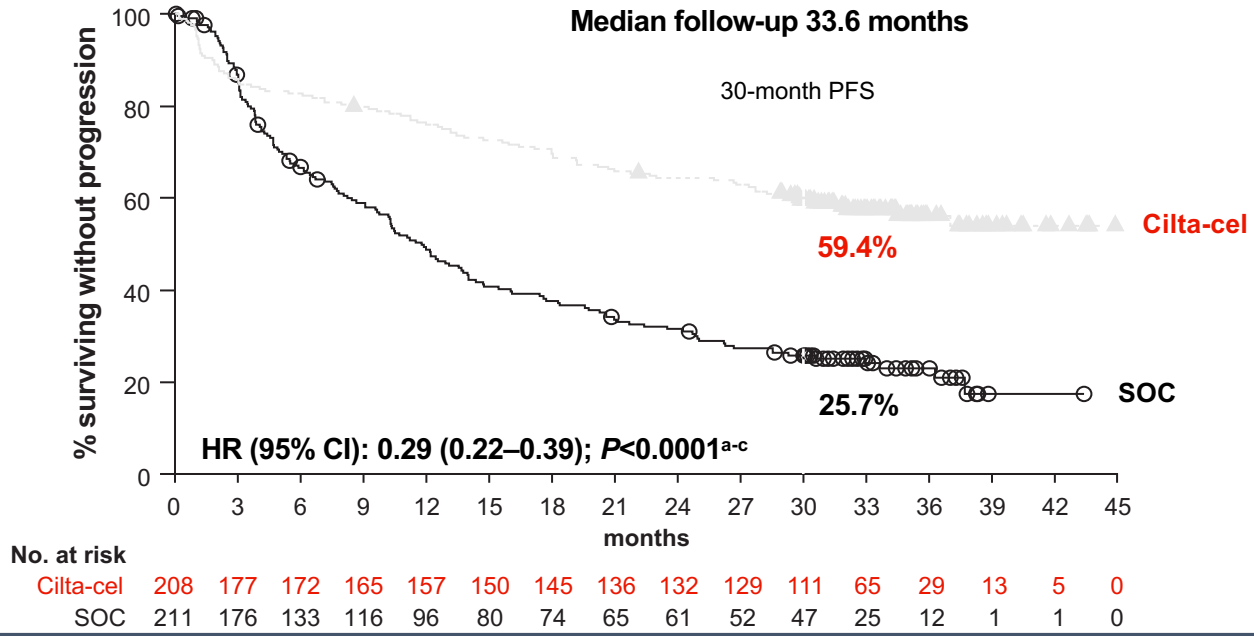


[a]Median follow-up, 15.9 months. [b]Constant piecewise weighted log-rank test. [c]HR and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable, including only PFS events that occurred >8 weeks post randomization.
cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; ITT, intent-to-treat; mPFS, median progression-free survival; NE, not estimable; SOC, standard of care.

Median follow-up was 15,4 months

Einsele H et al, EHA2023, San Miguel J et al NEJM 2023

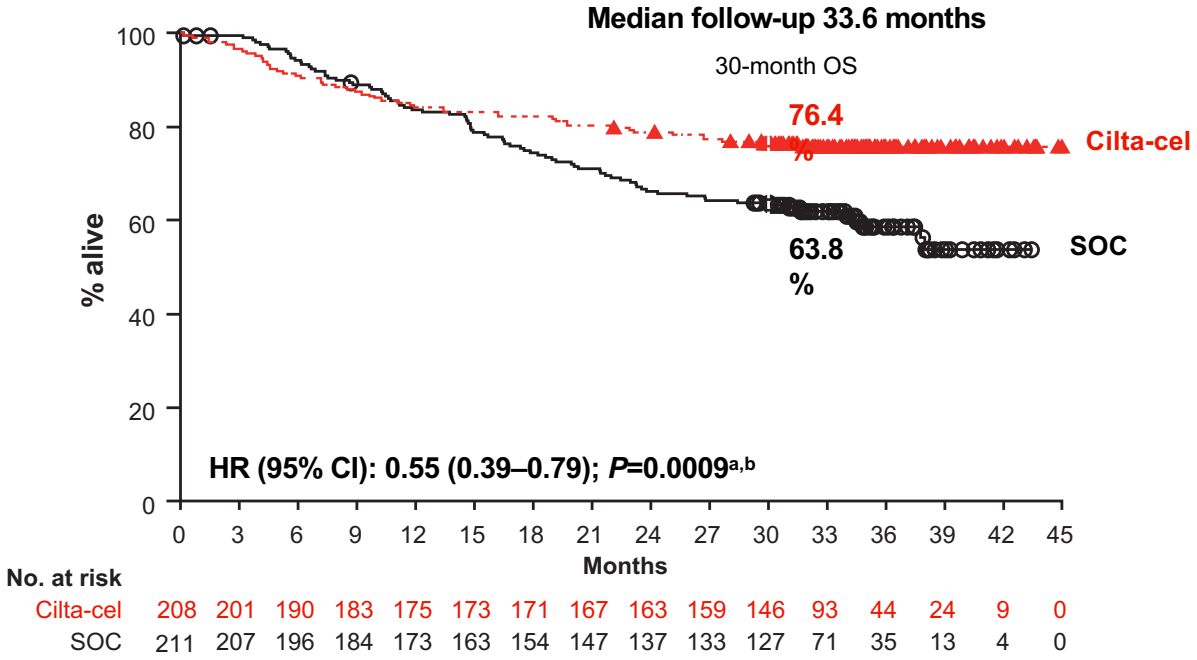
Long-Term CARTITUDE-4 Update (34 Months): Cilta-cel Maintained Significant Improvement in Progression-Free Survival



~70% reduction in the risk of progression or death in patients who received cilta-cel and mPFS has not been reached

Mateos MV, et al. IMS 2024 OA-65

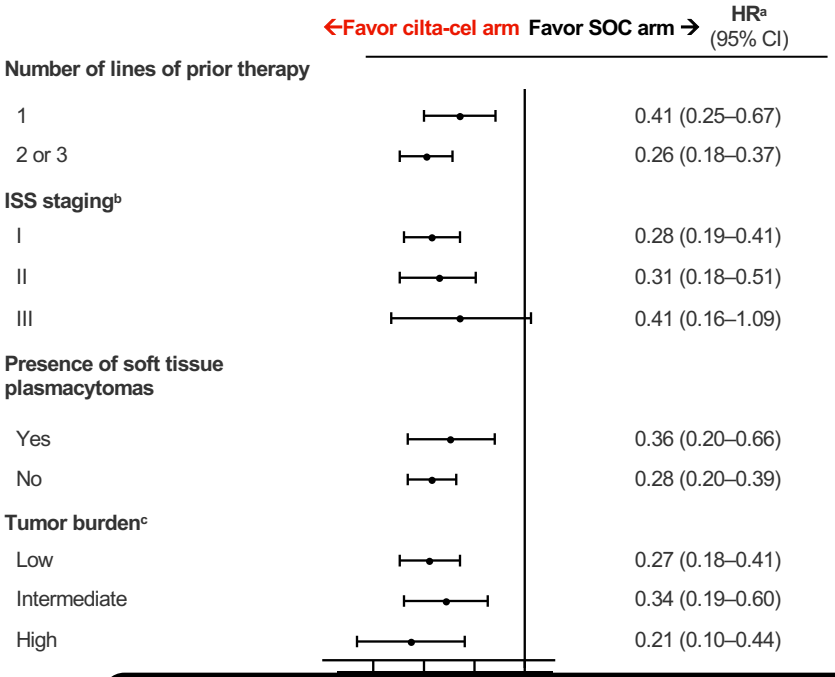
Long-Term CARTITUDE-4 Update (34 Months): Cilta-cel Significantly Improved Overall Survival

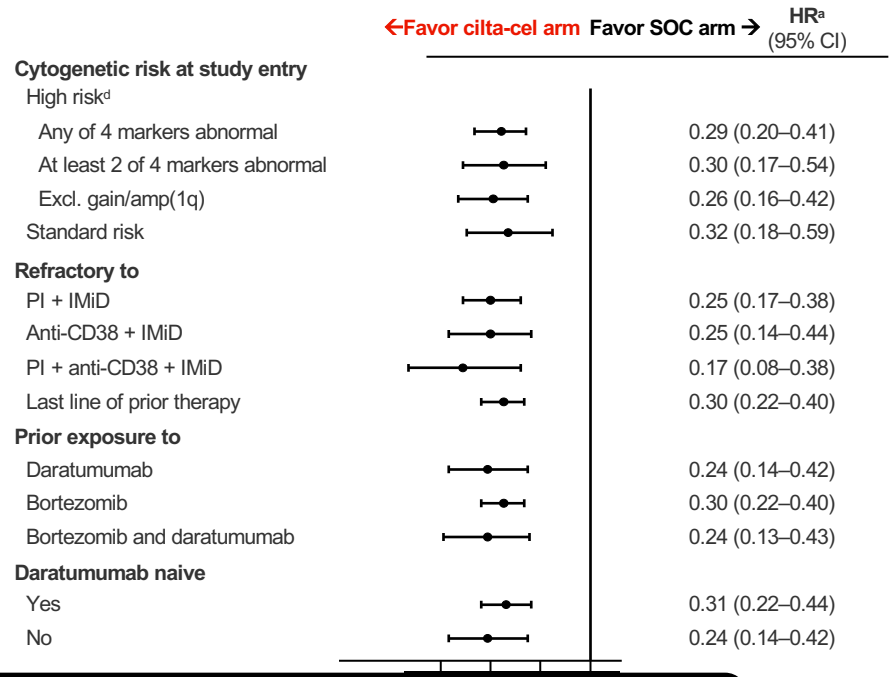


First CAR-T to demonstrate overall survival benefit in multiple myeloma

Mateos MV, et al. IMS 2024 OA-65

Long-Term CARTITUDE-4 Update (34 Months): Consistent Progression-Free Survival Benefit for Cilta-cel Across All Prespecified Subgroups

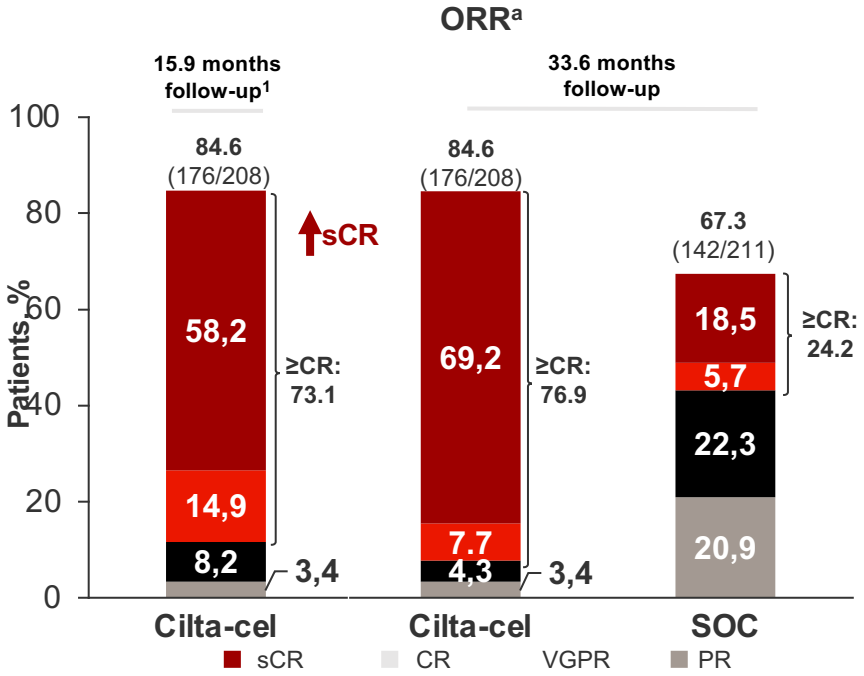




Consistent reduction in the risk of progression or death across all prespecified subgroups

Mateos MV, et al. IMS 2024 OA-65

Long-Term CARTITUDE-4 Update (34 Months): Increased Rates of Deep Responses Seen With Additional Follow-Up With Cilta-cel



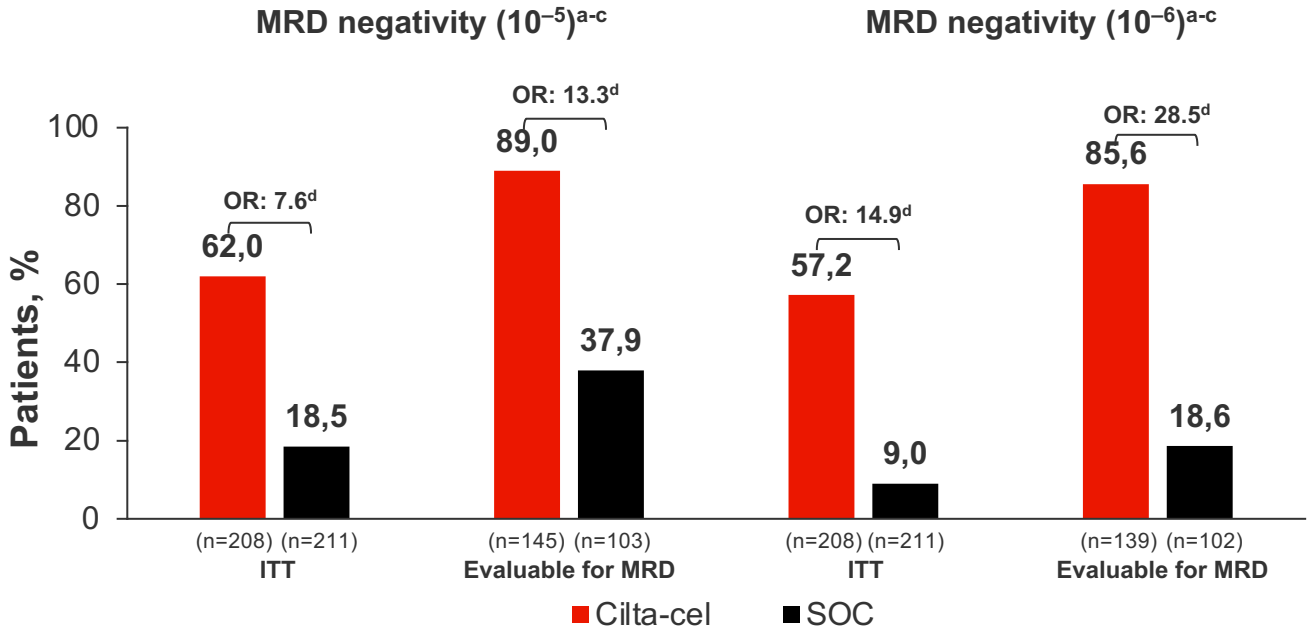
DOR[b]

	Cilta-cel	SOC
DOR, months, median (95% CI)	**NR (NE–NE)**	**18.7 (12.9–23.7)**
30-month DOR rate, % (95% CI)	67.4 (59.7–74.0)	35.5 (27.6–43.6)

Cilta-cel provided high ORR and sCR/CR rate with sustained DOR

Mateos MV, et al. IMS 2024 OA-65

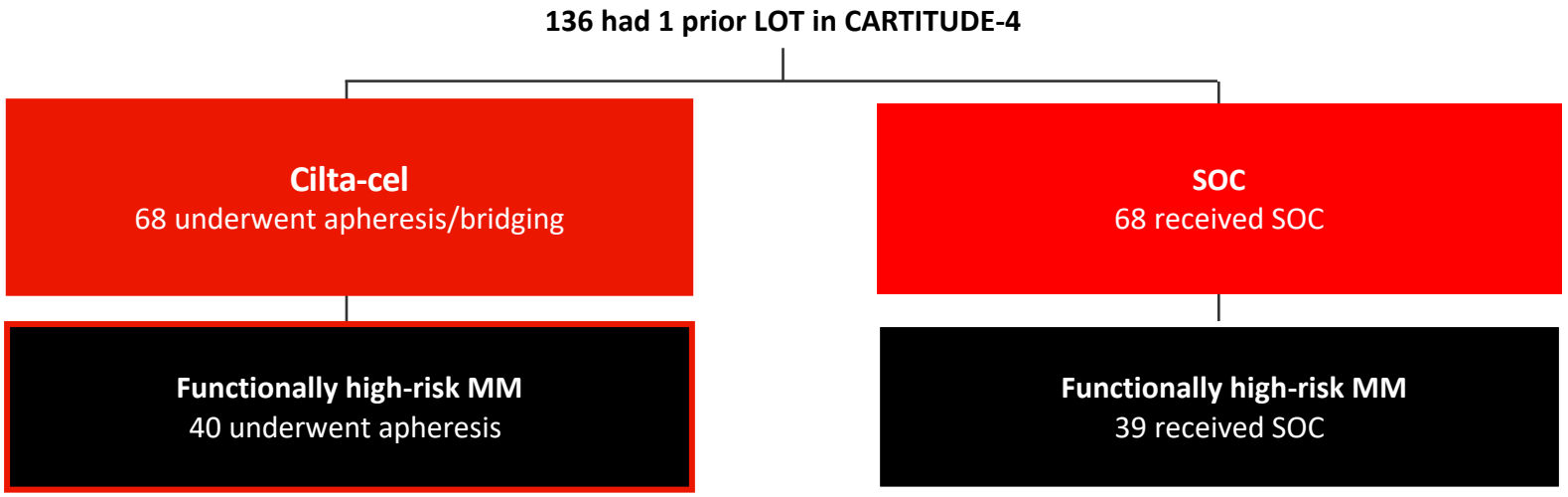
Long-Term CARTITUDE-4 Update (34 Months): Cilta-cel Provided Significantly Higher Rate of MRD Negativity



Cilta-cel increased MRD negativity more than 2-fold at 10^{-5}, and more than 4-fold at 10^{-6} vs SOC

Mateos MV, et al. IMS 2024 OA-65

CARTITUDE-4 Subgroup Analysis: Patient Population

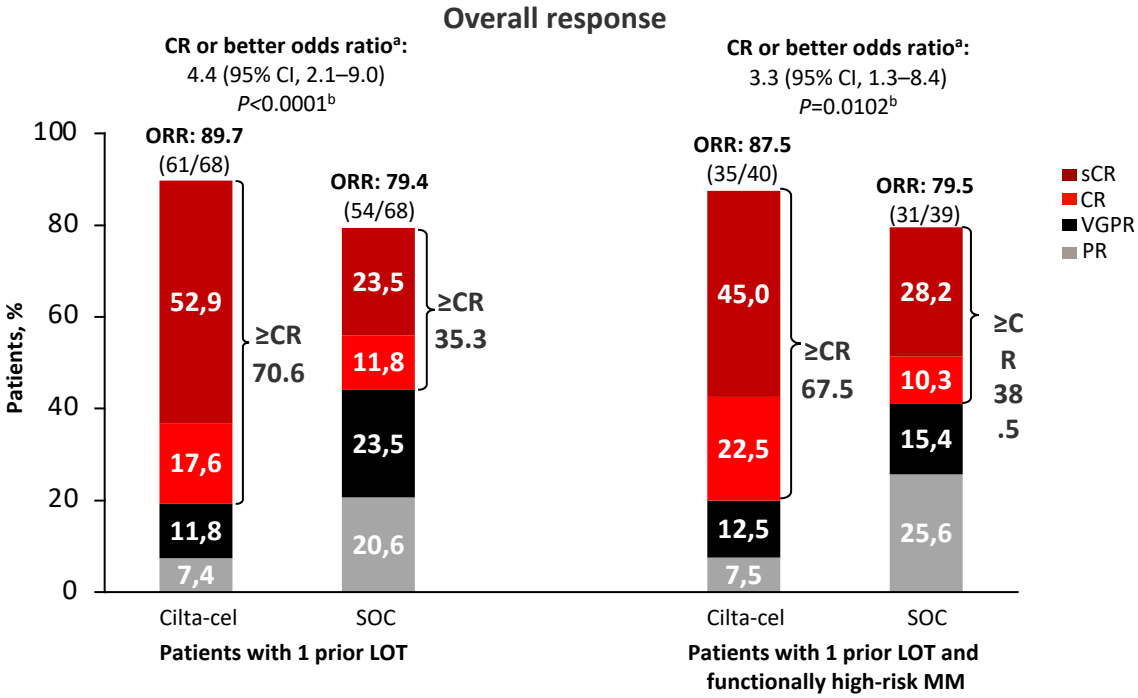


Functionally high-risk MM defined as PD ≤18 months after receiving ASCT or the start of initial frontline therapy in patients with no ASCT

At the November 2022, data cut-off date, median follow-up was 15.9 months (range, 0.1–27.3). Among 68 patients who received 1 prior LOT in the cilta-cel arm, 60 received cilta-cel as study treatment, 5 received cilta-cel as subsequent therapy, and 3 never received cilta-cel. Among 40 patients who received 1 prior LOT and functionally high-risk MM in the cilta-cel arm, 35 received cilta-cel as study treatment. Study treatment includes any portion of the following sequence: apheresis, bridging, lymphodepletion, and cilta-cel.
ASCT, autologous stem cell transplant; cilta-cel, ciltacabtagene autoleucel; LOT, line of therapy; MM, multiple myeloma; PD, progressive disease; SOC, standard of care.

Weisel, et al. ORAL P959 EHA 2024

CARTITUDE-4 Subgroup Analysis: Consistently Deeper Responses Achieved With Cilta-cel vs SOC in Patients With 1 Prior LOT and Those With 1 Prior LOT and Functionally High-Risk MM



Treatment response was assessed by a validated computerized algorithm, based on International Myeloma Working Group consensus criteria. ORR was defined as the proportion of patients who achieve a PR or better.
[a]Mantel-Haenszel estimate of the common odds ratio for unstratified tables is used. [b]*P* value from the Cochran-Mantel-Haenszel chi-squared test. cilta-cel, ciltacabtagene autoleucel; CR, complete response; LOT, line of therapy; MM, multiple myeloma; ORR, overall response rate; PR, partial response; sCR, stringent complete response; SOC, standard of care; VGPR, very good partial response.

Weisel, et al. ORAL P959 EHA 2024

219 BMS-986393 (CC-95266), a G Protein–Coupled Receptor Class C Group 5 Member D (GPRC5D)–Targeted Chimeric Antigen Receptor (CAR) T-Cell Therapy for Relapsed/Refractory Multiple Myeloma (RRMM): Updated Results from a Phase 1 Study

CC-95266-MM-001 (NCT04674813), a phase 1, first-in-human, multicenter, open-label, dose-finding study evaluating BMS-986393 (CC-95266), a GPRC5D-targeted autologous CAR T-cell therapy,

in pts with RRMM who had received ≥ 3 prior treatment regimens and must have received a PI, a Imids, an anti-CD38 therapy, and an ASCT (if eligible); prior BCMA-directed and CAR T-cell therapies were allowed.

Escalating doses up 450 × 10^6 CAR T cells

Bal S et al. ASH 2023

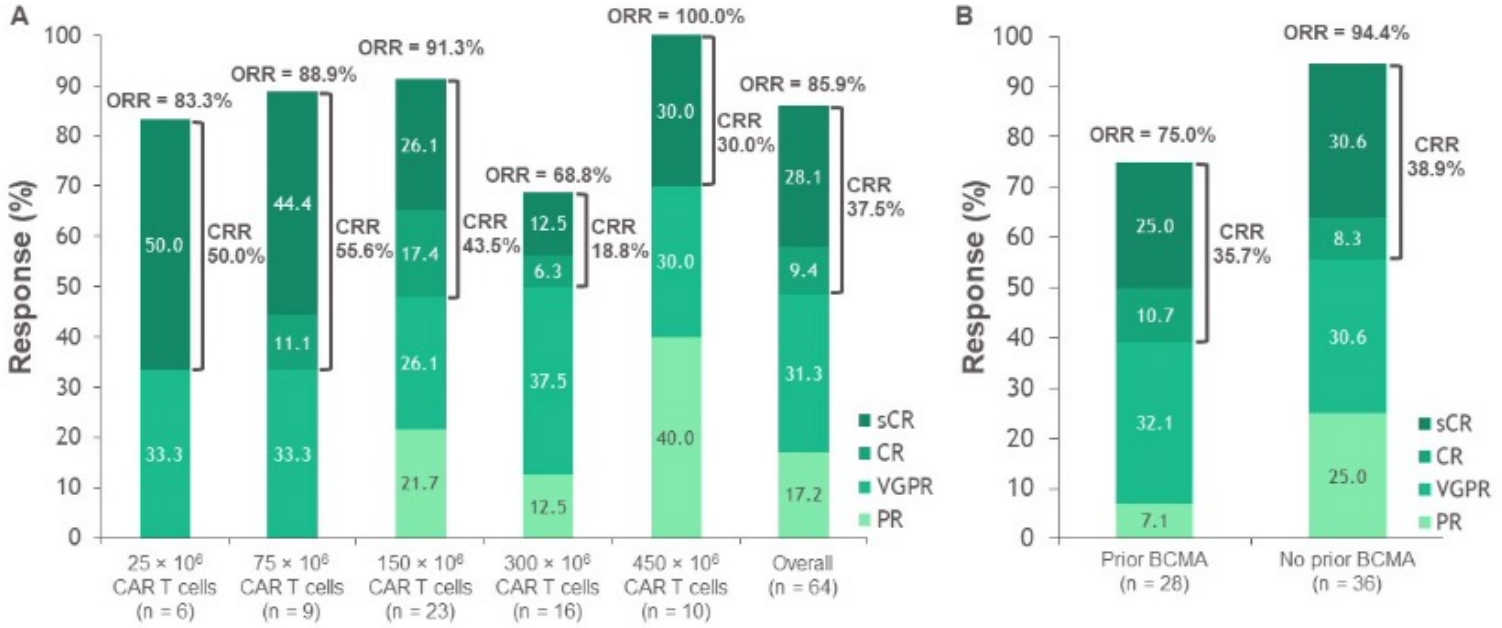
70 patients

- 46% with high-risk cytogenetics;
- 43% extramedullary MM
- 34% penta-drug refractory;
- 43% prior BCMA-directed therapies

CRS and ICANS were mostly low-grade, with increased G ≥ 3 events at the 300 and 450 $\times 10^6$ CAR T-cell doses.

On-target off-tumor TRAEs, all G1/2, occurred in a minority of pts

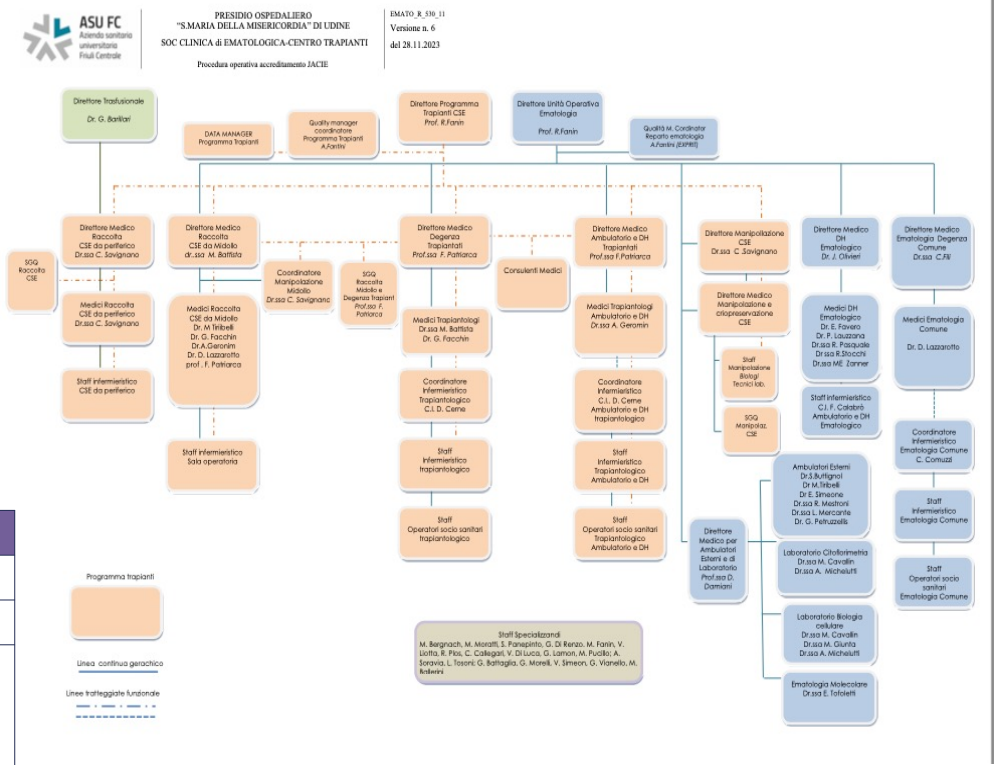
Figure. Best overall response (A) by dose level and (B) according to prior BCMA treatment (efficacy-evaluable analysis set)[a].



Conclusions

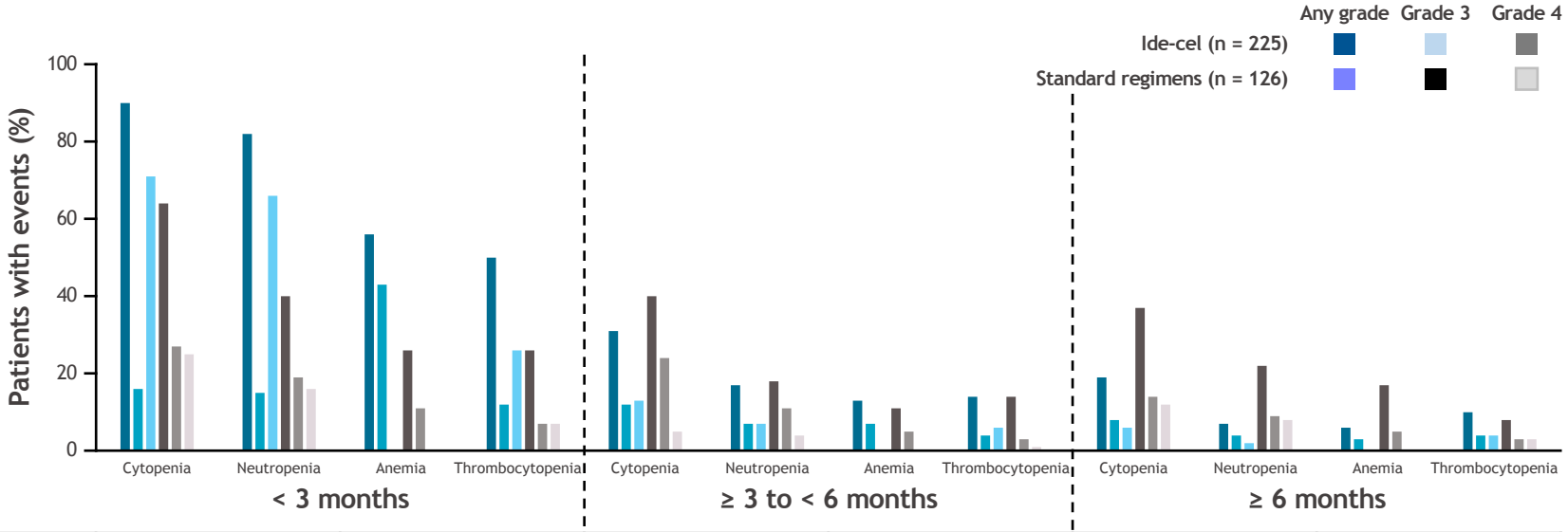
- Real word data confirmed efficacy and manageble toxicities already shown by registrative studies.
- Hematotox and Mycare scores coud be useful for identifying suitable candidates for CAR-T in the setting of triple exposed MM.
- Ide-cel was superior to ST in pts who had received 2-4 lines of treatment, including Daratumumab (mPFS 13.3 vs 4.4 months).
- Cilta-cel was superior to ST in pts who had receive 1-3 lines, daratumumab only 20% (30 months- PFS 59% vs 25%, OS advantage).
- Initial data in patients in second-line therapy (inadequate response to ASCT, functional high-risk myeloma) are promising.

	2022	2023	2024*
N° pazienti	9	9	25
Età mediana (range)	**69 (42-77)**	**57 (48-77)**	**65 (37-78)**
Indicazione			
• **DLBCL**	**5 (56%)**	**5 (56%)**	**14 (56%)**
• PMBCL	1 (11%)	1 (11%)	0
• MCL	1 (11%)	3 (33%)	2 (8%)
• FL	0	1 (11%)	6 (24%)
• LAL	1 (11%)	0	3 (12%)
2° linea/ >2° linea	0/9	0/9	9/16
Prodotto:			
• Tisa-cel	5 (56%)	2 (22%)	7 (28%)
• **Axi-cel**	2 (22%)	5 (56%)	13 (52%)
• **Brexu-cel**	2 (22%)	2 (22%)	5 (20%)
Δt aferesi-infusione (giorni)	42 (33-62)	42,5 (31-94)	45 (35-70)



Grazie!

Summary of incidence and management of cytopenia



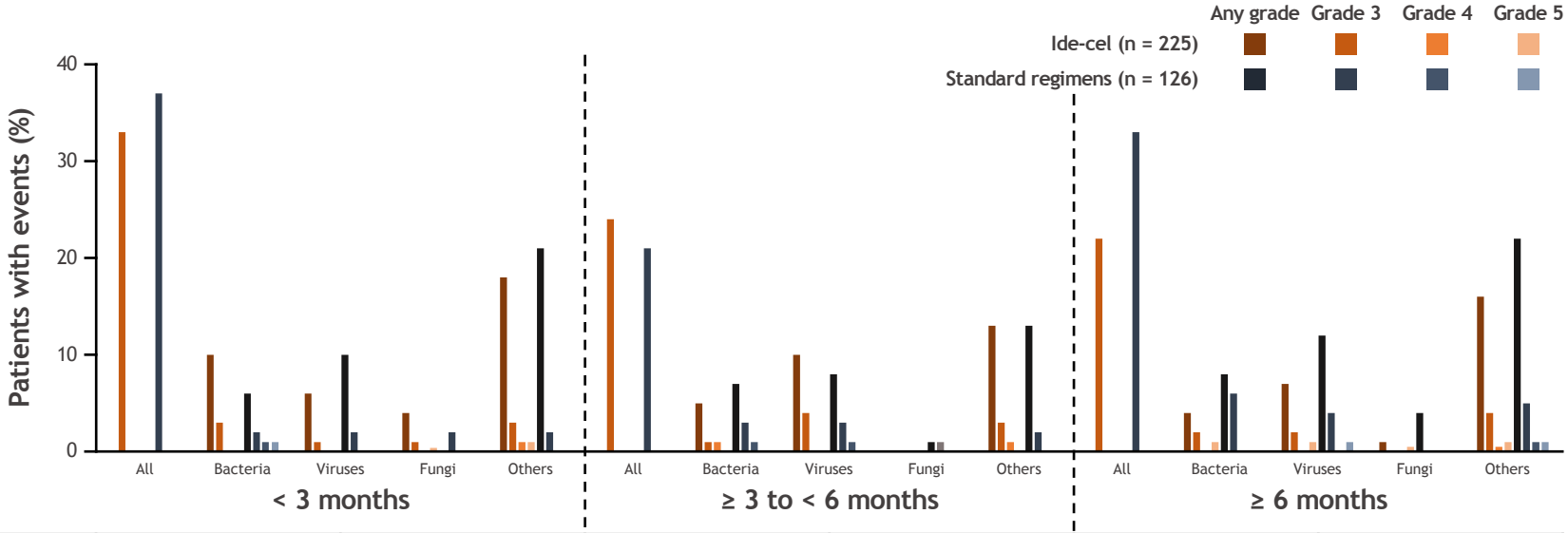
Patients remaining on time interval	Ide-cel (n = 225)	Standard regimens (n = 126)	Ide-cel (n = 216)	Standard regimens (n = 106)	Ide-cel (n = 204)	Standard regimens (n = 78)
CSF	114 (51)	30 (24)	19 (9)	7 (7)	6 (3)	7 (9)
RBC transfusion	62 (28)	10 (8)	11 (5)	2 (2)	8 (4)	2 (3)
Platelet transfusion	39 (17)	3 (2)	12 (6)	0	6 (3)	1 (1)
TPO mimetics	4 (2)	2 (2)	1 (<1)	0	0	0
CD34+ stem cell boost	1 (< 1)	0	0	0	0	0

Data are in n (%). CSF includes filgrastim, filgrastim AAFI, filgrastim SNDZ, granulocyte colony-stimulating factor, lenograstim, lipegfilgrastim, pegfilgrastim, pegfilgrastim BMEZ, pegfilgrastim CBQV, pegfilgrastim JMDB, and TBO filgrastim.

CD, cluster of differentiation; CSF, colony-stimulating factor; ide-cel, idecabtagene vicleucel; RBC, red blood cell; TPO, thrombopoietin.

Baz et al, 4879

Summary of incidence and management of infections



Patients remaining on time interval	Ide-cel (n = 225)	Standard regimens (n = 126)	Ide-cel (n = 216)	Standard regimens (n = 106)	Ide-cel (n = 204)	Standard regimens (n = 78)
Antibiotics	41 (18)	29 (23)	36 (17)	16 (15)	30 (15)	14 (18)
Antivirals	6 (3)	3 (2)	7 (3)	3 (3)	5 (2)	3 (4)
Antifungals	1 (< 1)	0	0	0	3 (1)	0

Baz et al, 4879

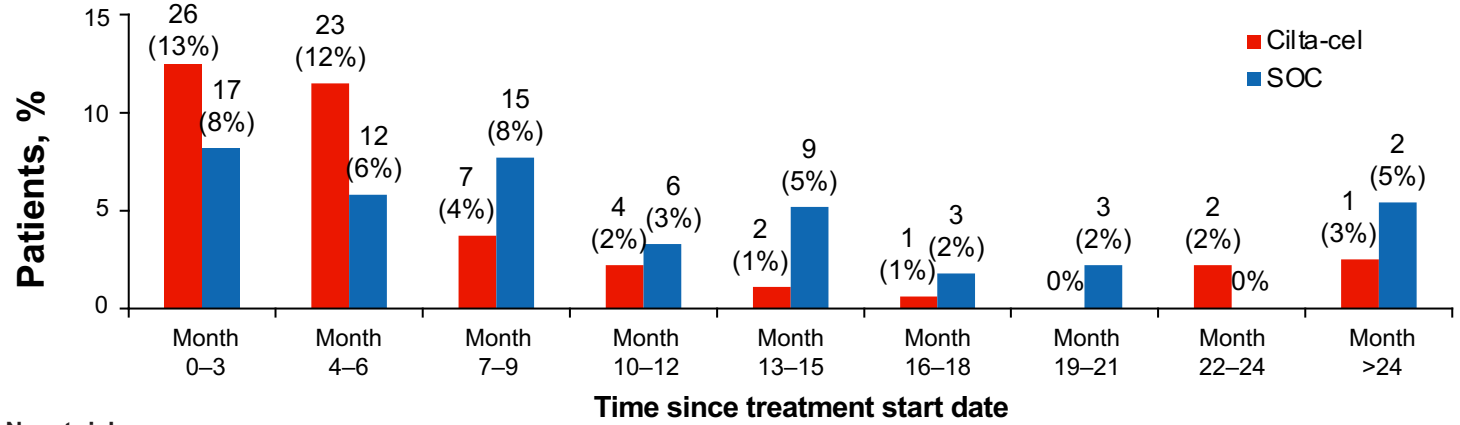
Summary of incidence of SPM

SPM category SPM subcategory Preferred term	Ide-cel (n = 225)		Standard regimens (n = 126)	
	All, n (%)	Incidence per 100 person-years, % (95% CI)	All, n (%)	Incidence per 100 person-years, % (95% CI)
Any SPM	15 (7)	4 (2.4–6.7)	5 (4)	4 (1.9–10.7)
Invasive SPM	11 (5)	3 (1.6–5.3)	3 (2)	3 (1.0–8.1)
Hematologic malignancy	5 (2)	1 (0.5–3.1)	0	0
Myelodysplastic syndrome	4 (2)	–	0	–
Acute myeloid leukemia	1 (< 1)	–	0	–

Ide-cel, idecabtagene vicleucel; SPM, second primary malignancy.

Baz R et al, 4879

CARTITUDE 4: Grade ≥3 TE infections



No. at risk									
Cilta-cel	208	200	188	182	175	173	147	90	40
SOC	208	206	194	184	173	163	134	81	37