CART & BisAb – meeting highlights

יעל כהן

מרכז רפואי תל אביב סוראסקי (איכילוב)

מפגש החוג למיאלומה 11.11.2024

Talquetamab + Daratumumab + Pomalidomide in Patients With Relapsed/Refractory Multiple Myeloma: Results From the Phase 1b TRIMM-2 Study

Nizar Bahlis[1], Niels WCJ van de Donk[2], Donna Reece[3], Manisha Bhutani[4], Bhagirathbhai Dholaria[5], Anita D'Souza[6], Thomas G Martin[7], John McKay[8], Alfred Garfall[9], Amrita Krishnan[10], Kalpana Bakshi[11], Lijuan Kang[11], Lien Vandenberk[12], Thomas Prior[11], Jaszianne Tolbert[11], Ajai Chari[13]

Key eligibility criteria

- MM per IMWG
- ≥3 prior LOT[a] or double refractory to PI and IMiD
- Permitted:
  - Anti-CD38 mAb >90 days and IMiD >7 days prior
  - Refractory to anti-CD38 mAb
  - Prior bispecific antibody or CAR-T exposure

Tal[b] + **Dara[c]** **1800 mg SC** + **Pom** **2 mg PO**

Tal[b]	Dara[c] 1800 mg SC	Pom 2 mg PO
SUD followed by 0.4 mg/kg SC QW or 0.8 mg/kg SC Q2W	QW cycles 1–2 Q2W cycles 3–6 Q4W cycles ≥7	Starting cycle 2
May change schedule from QW to Q2W after cycle 4 if in PR and from Q2W to Q4W after cycle 8 if in VGPR		*May be reduced in response to hematologic AEs*

Key objectives

- Safety and antitumor activity

TRIMM-2 Tal + Dara + Pom Cohort: Majority of Patients Dara And Pom Refractory

Characteristic	Tal 0.4 mg/kg QW + dara + pom (n=18)	Tal 0.8 mg/kg Q2W + dara + pom (n=59)
Age (years), median (range)	62 (42–75)	64 (33–81)
Male, n (%)	12 (66.7)	31 (52.5)
Race, n (%)		
White	12 (66.7)	51 (86.4)
Black/African American	4 (22.2)	4 (6.8)
Asian	1 (5.6)	1 (1.7)
American Indian/Alaska Native	0 (0)	1 (1.7)
Not reported	1 (5.6)	2 (3.4)
Soft tissue plasmacytoma(s),[a] n (%)	4 (22.2)	14 (23.7)
High cytogenetic risk,[b] n (%)	4 (22.2)	13 (27.7)
ISS stage,[c] n (%)		
I	8 (50.0)	29 (52.7)
II	3 (18.8)	15 (27.3)
III	5 (31.3)	11 (20.0)
Time since diagnosis (years), median (range)	5.7 (0.3–18.3)	7.2 (0.7–17.5)

Characteristic	Tal 0.4 mg/kg QW + dara + pom (n=18)	Tal 0.8 mg/kg Q2W + dara + pom (n=59)
Prior LOT (n), median (range)	6 (3–11)	6 (1–17)
Prior stem cell transplantation, n (%)	16 (88.9)	50 (84.7)
Prior therapies, n (%)		
Anti-CD38	17 (94.4)	55 (93.2)
IMiD	18 (100.0)	59 (100.0)
Triple class[d]	17 (94.4)	55 (93.2)
Penta drug[e]	12 (66.7)	41 (69.5)
BCMA-targeted therapy	13 (72.2)	40 (67.8)
CAR-T	5 (27.8)	19 (32.2)
Bispecific antibody[f]	6 (33.3)	17 (28.8)
ADC	3 (16.7)	12 (20.3)
Refractory status, n (%)		
Anti-CD38[g]	15 (83.3)	49 (83.1)
Pom	13 (72.2)	45 (76.3)
Triple class[d]	15 (83.3)	45 (76.3)
Penta drug[e]	4 (22.2)	20 (33.9)
Any prior bispecific antibody	7 (38.9)	22 (37.3)
To last line of therapy	17 (94.4)	53 (89.8)

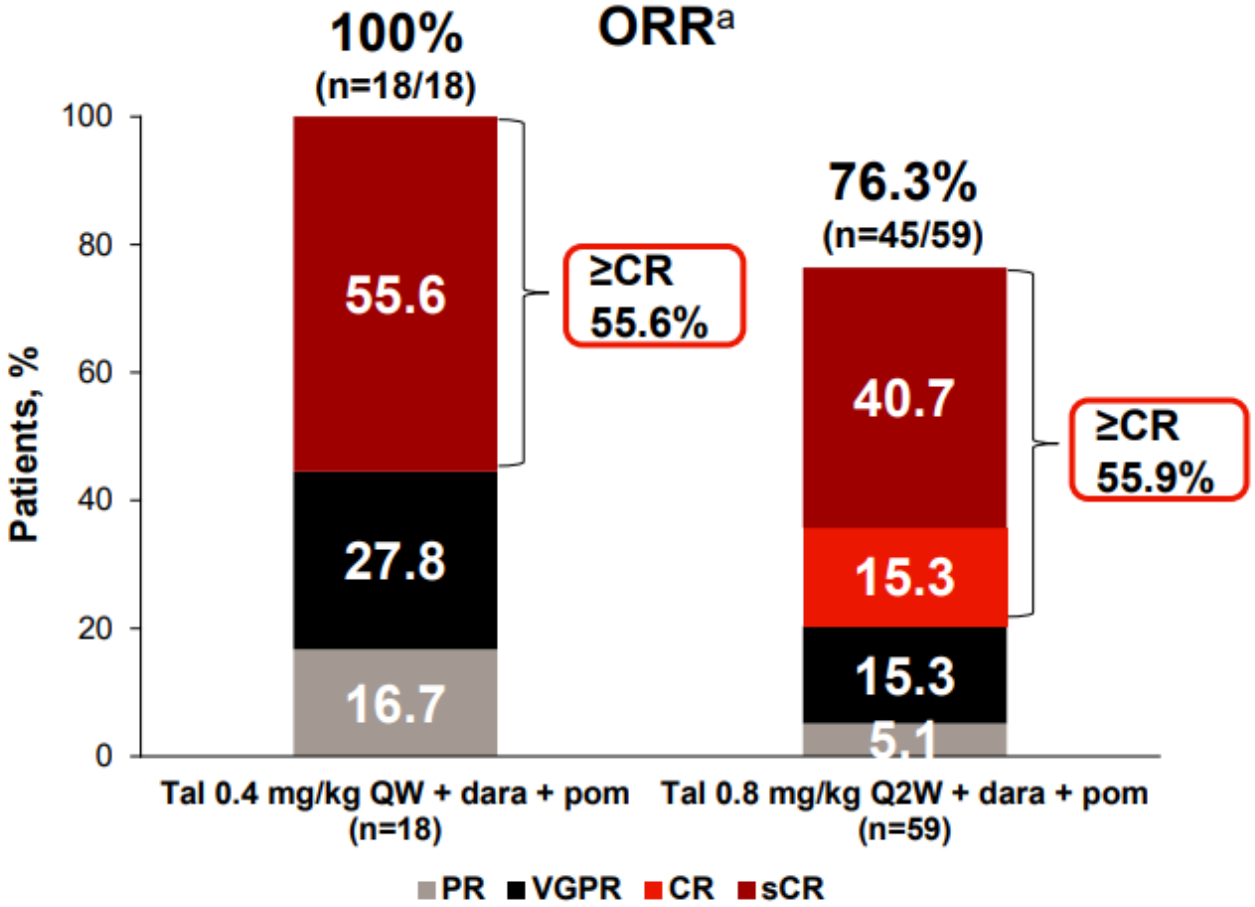
Data cut-off: July 29, 2024. [a]Soft tissue plasmacytomas not associated with the bone were included. [b]del(17p), t(4;14), and/or t(14;16); percentages calculated from n=18 for tal QW and n=47 for tal Q2W. [c]Percentages calculated from n=16 for tal QW and n=55 for tal Q2W. [d]≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 mAb. [e]≥2 PIs, ≥2 IMiDs, and ≥1 anti-CD38 mAb. [f]6 patients received non-BCMA–directed bispecific antibodies. [g]All patients in the tal QW cohort received dara; in the tal Q2W cohort, 89.8% received dara, 13.6% received isatuximab, and 1.7% received other anti-CD38 therapies. ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; dara, daratumumab; IMiD, immunomodulatory drug; ISS, International Staging System; LOT, line of therapy; mAb, monoclonal antibody; PI, proteasome inhibitor; pom, pomalidomide; Q2W, every other week; QW, weekly; tal, talquetamab.

Presented by N Bahlis at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

TRIMM-2 Tal + Dara + Pom Cohort: SAFETY

- Grade 3/4 Infection Rate Generally Low (16-37%) Despite Neutropenia Being Common
- Nonhematologic AEs Consistent With Profile of Individual Agents
- Discontinuation of ≥1 drug due to AEs – 27.8% (QW) and 47.5% (Q2W)
- 2 deaths due to AEs
- Taste, skin, and nail AEs mostly low grade; no discontinuations – Rash in 27.8% (QW) and 25.4% (Q2W) of patients

TRIMM-2 Tal + Dara + Pom Cohort: Combined ORR 82% and ≥CR Rate 56%

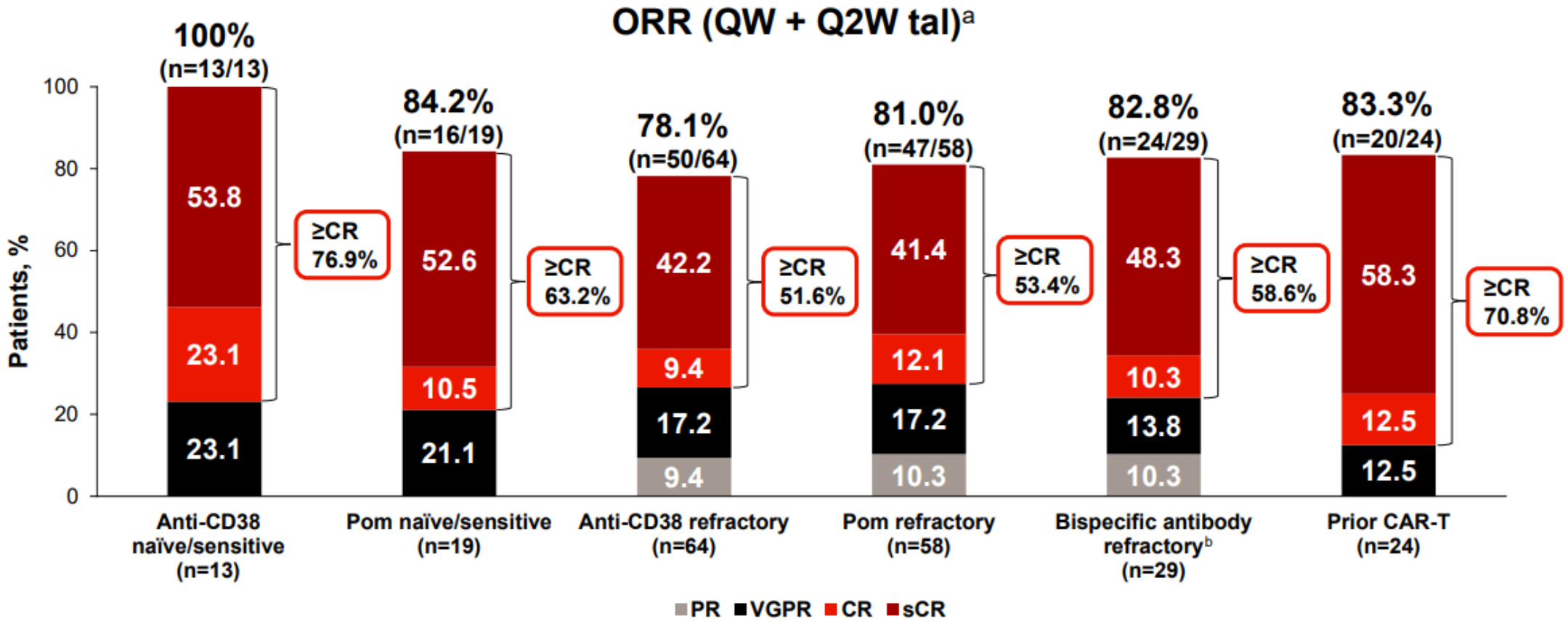


	Tal 0.4 mg/kg QW + dara + pom (n=18)	Tal 0.8 mg/kg Q2W + dara + pom (n=59)
Median (range) follow-up, months	15.8 (3.2–37.9)	17.5 (0.2–37.7)
Median (range) time to first response, months	1.0 (0.9–3.6)	1.0 (0.9–6.7)
Combined ORR, % (n/N)	**81.8** (63/77)	
Combined ≥CR, % (n/N)	**55.8** (43/77)	

Data cut-off: July 29, 2024.
[a]Response was assessed by investigators, based on IMWG criteria. Percentages are calculated with the number of patients in each group as denominator.
CR, complete response; dara, daratumumab; IMWG, International Myeloma Working Group; ORR, overall response rate; pom, pomalidomide; PR, partial response; Q2W, every other week; QW, weekly; sCR, stringent complete response; tal, talquetamab; VGPR, very good partial response.

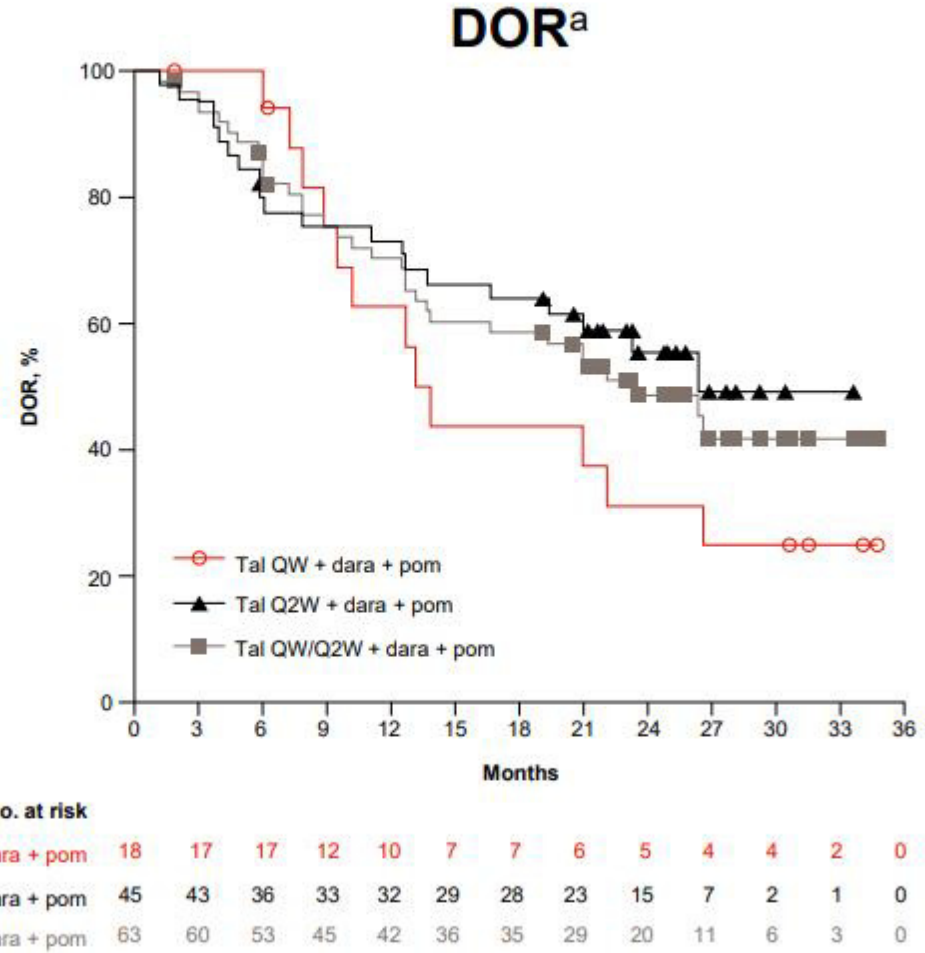
Presented by N Bahlis at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

TRIMM-2 Tal + Dara + Pom Cohort: High ORRs in Prior Exposure Subgroups



Data cut-off: July 29, 2024

TRIMM-2 Tal + Dara + Pom Cohort: Durable Responses, Including in Key Exposure Subgroups



Parameter	Tal 0.4 mg/kg QW + dara + pom (n=18)	Tal 0.8 mg/kg Q2W + dara + pom (n=45)
Median (range) follow-up, months	15.8 (3.2–37.9)	17.5 (0.2–37.7)
Median DOR, months (95% CI)	13.8 (8.8–26.6)	26.4 (16.7–NE)
12-month DOR, % (95% CI)	62.7 (35.1–81.3)	73.1 (57.5–83.7)

12-month DOR (QW + Q2W tal)

- Anti-CD38 naïve/sensitive (n=13): 83.9%
- Pom naïve/sensitive (n=16): 80.8%
- Anti-CD38 refractory (n=50): 67.0%
- Pom refractory (n=47): 67.0%
- Bispecific antibody refractory (n=24): 70.2%
- Prior CAR-T (n=20): 84.4%

Data cut-off: July 29, 2024.
Anti-CD38 naïve = never received anti-CD38 therapy; anti-CD38 sensitive = minimal response or better during treatment; anti-CD38 refractory = best response of SD or PD during treatment or within 60 days of completing anti-CD38 therapy. [a]Response and progression were assessed by investigators, based on IMWG criteria. CAR, chimeric antigen receptor; dara, daratumumab; DOR, duration of response; IMWG, International Myeloma Working Group; NE, not evaluable; PD, progressive disease; pom, pomalidomide; Q2W, every other week; QW, weekly; SD, stable disease; tal, talquetamab.

Presented by N Bahlis at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

Talquetamab + Teclistamab in Patients With Relapsed/Refractory Multiple Myeloma: Updated Phase 1b Results From RedirecTT-1 With >1 Year of Follow-Up

Yaël C Cohen[1], Hila Magen[2], Moshe Gatt[3], Michael Sebag[4], Kihyun Kim[5], Chang-Ki Min[6], Enrique M Ocio[7], Sung-Soo Yoon[8], Michael P Chu[9], Paula Rodríguez-Otero[10], Irit Avivi[1], Natalia A Quijano Cardé[11], Maria Krevvata[11], Michelle R Peterson[11], Emma Scott[11], Brandi W Hilder[11], Jill Vanak[11], Arnob Banerjee[11], Albert Oriol[12], Daniel Morillo[13], María-Victoria Mateos[14]

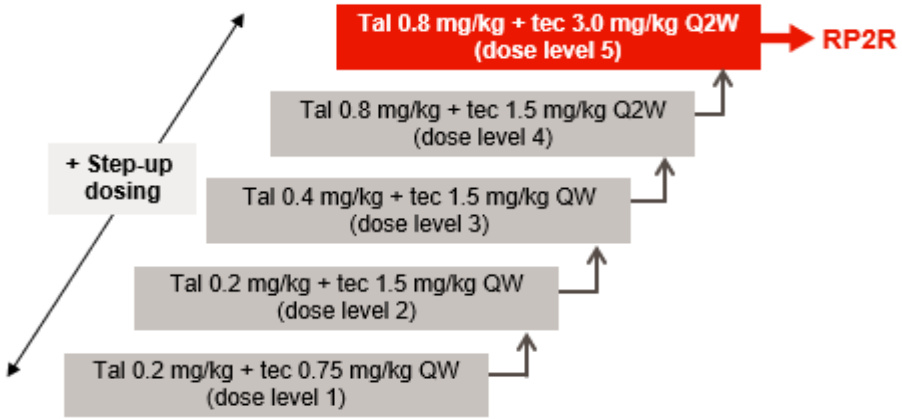
Key eligibility criteria

- Measurable MM
- EMD permitted (≥1 nonradiated, bone-independent lesion ≥2 cm)
- RR or intolerant to established therapies, including last LOT
- Triple-class exposed (prior PI, IMiD, anti-CD38)

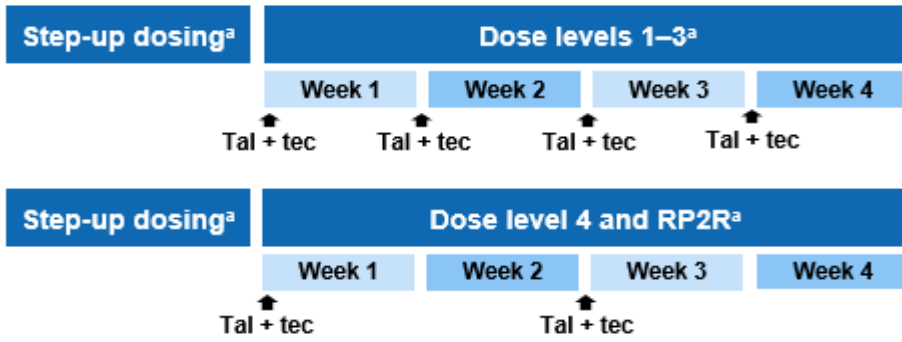
Key objectives

- Safety, including DLTs
- Identify RP2R(s)
- ORR, DOR, time to response, PK, immunogenicity
- PFS

Phase 1 dose escalation



Dosing schedule



Patients could transition from QW to Q2W and from Q2W to Q4W dosing after achieving a ≥PR after cycle 4

RedirecTT-1 Tal + Tec: Heavily Pretreated and a High Proportion of EMD

Characteristic	RP2R (n=44)	All doses (N=94)
Median age, years (range)	63.0 (41–80)	64.5 (39–81)
Male, n (%)	23 (52.3)	49 (52.1)
Race, n (%)		
White	32 (72.7)	75 (79.8)
Black/African American	0 (0)	1 (1.1)
Asian	12 (27.3)	17 (18.1)
Unknown	0 (0)	1 (1.1)
Extramedullary plasmacytomas ≥1,[a] n (%)	18 (40.9)	34 (36.2)
High-risk cytogenetics,[b] n (%)	8 (42.1)	21 (41.2)
ISS stage,[c] n (%)		
I	19 (46.3)	38 (44.7)
II	14 (34.1)	26 (30.6)
III	8 (19.5)	21 (24.7)
Years since diagnosis, median (range)	5.5 (0.3–12.9)	6.1 (0.3–14.6)

Characteristic	RP2R (n=44)	All doses (N=94)
Median prior LOT, n (range)	4.0 (2–10)	4.0 (1–11)
Exposure status, n (%)		
Belantamab mafodotin	5 (11.4)	18 (19.1)
CAR-T therapy[d]	2 (4.5)	4 (4.3)
Bispecific antibody[e]	2 (4.5)	7 (7.4)
Any BCMA-directed therapy	9 (20.5)	27 (28.7)
Triple-class	44 (100.0)	94 (100.0)
Penta-drug	28 (63.6)	61 (64.9)
Refractory status, n (%)		
Proteasome inhibitor	41 (93.2)	85 (90.4)
Immunomodulatory drug	41 (93.2)	91 (96.8)
Anti-CD38	43 (97.7)	93 (98.9)
Triple-class	37 (84.1)	81 (86.2)
Penta-drug	13 (29.5)	31 (33.0)
To last line of therapy	39 (88.6)	87 (92.6)

Triple-class exposed population, 36% with extramedullary plasmacytomas

Data cut-off date: March 15, 2024. Percentages were calculated with the number of patients with available data as the denominator. [a]≥1 nonradiated, bone-independent lesion ≥2 cm. Patients with paraskeletal plasmacytomas were permitted but not counted as EMD. [b]FISH or karyotype testing in n=51 (all doses) and n=19 (RP2R). Defined as del(17p), t(4;14), or t(14;16). [c]In n=85 (all doses) and n=41 (RP2R). [d]Across all doses: BCMA-directed CAR-T (n=2) and not specified (n=2). [e]Across all doses: alnuctamab (n=4), WV-T078 (n=2), and teclistamab (n=1). BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; EMD, extramedullary disease; FISH, fluorescence in situ hybridization; ISS, International Staging System; LOT, line of therapy; RP2R, recommended phase 2 regimen; tal, talquetamab; tec, teclistamab.

Presented by YC Cohen at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

RedirecTT-1 Tal + Tec: Safety Consistent With Known Profiles of Tal and Tec

Most common AEs (≥35% overall),[a] n (%)	RP2R (n=44)		All doses (N=94)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
CRS	33 (75.0)	0 (0)	74 (78.7)	2 (2.1)
Taste changes[b]	22 (50.0)	NA	61 (64.9)	NA
Non-rash skin AEs[c]	25 (56.8)	0 (0)	57 (60.6)	0 (0)
Nail-related AEs[d]	21 (47.7)	0 (0)	49 (52.1)	0 (0)
Pyrexia	14 (31.8)	1 (2.3)	48 (51.1)	2 (2.1)
Diarrhea	21 (47.7)	2 (4.5)	45 (47.9)	3 (3.2)
Cough	13 (29.5)	0 (0)	42 (44.7)	1 (1.1)
Dry mouth	18 (40.9)	0 (0)	40 (42.6)	0 (0)
COVID-19	21 (47.7)	6 (13.6)	38 (40.4)	17 (18.1)
Rash AEs[e]	14 (31.8)	1 (2.3)	37 (39.4)	1 (1.1)
Pneumonia	14 (31.8)	7 (15.9)	34 (36.2)	19 (20.2)

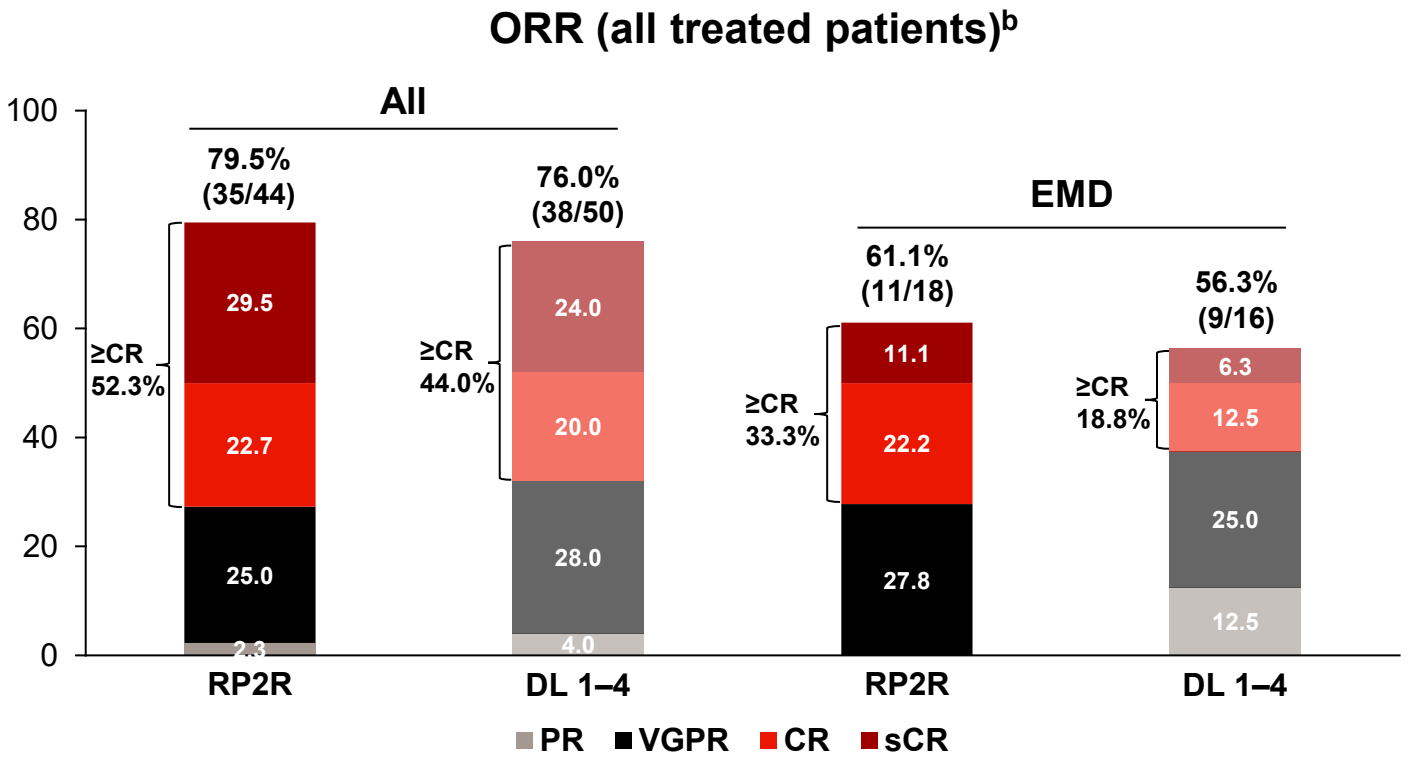
- 3 DLTs: oral herpes (dose level 1), elevated ALT/AST (dose level 3), and thrombocytopenia (RP2R)
- Discontinuations due to AEs:
  - 13.6% (n=6; RP2R), 16.0% (n=15; all doses)
- Grade 5 AEs:
  - 11.4% (n=5; RP2R), 14.9% (n=14; all doses)
  - Most (11/14) due to infections

Consistent safety profile between RP2R and all doses

Data cut-off date: March 15, 2024. Median follow-up: 18.2 months (RP2R) and 20.3 months (all doses).
[a]AEs graded by CTCAE v5.0; CRS per ASTCT criteria. [b]Includes dysgeusia, ageusia, hypogeusia, and taste disorder; maximum grade for taste changes is 2 per CTCAE. [c]Includes skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [d]Includes nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. [e]Includes rash, maculopapular rash, erythematous rash, and erythema. AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DLT, dose-limiting toxicity; NA, not applicable; RP2R, recommended phase 2 regimen; tal, talquetamab; tec, teclistamab.

Presented by YC Cohen at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

RedirecTT-1 Tal + Tec: High ORR and Deep Responses, Including in EMD[a]



All patients	RP2R (n=44)	DL 1–4 (n=50)
Median (range) follow-up, months	18.2 (0.7–27.0)	29.0 (0.5[c]–37.1)
Median (range) time to first response, months	1.4 (0.3–5.1)	2.1 (1.1–7.7)
Median (range) time to best response, months	4.9 (1.4–19.8)	4.9 (1.1–30.6)

Patients with EMD	RP2R (n=18)	DL 1–4 (n=16)
Median (range) follow-up, months	13.6 (0.7–25.9)	18.7 (0.5[c]–33.8)
Median (range) time to first response, months	3.0 (1.4–5.1)	2.6 (2.1–3.8)
Median (range) time to best response, months	6.3 (3.0–10.7)	3.9 (2.1–10.7)

ORR 79.5% (61.1% in EMD) at RP2R with rapid and deep responses

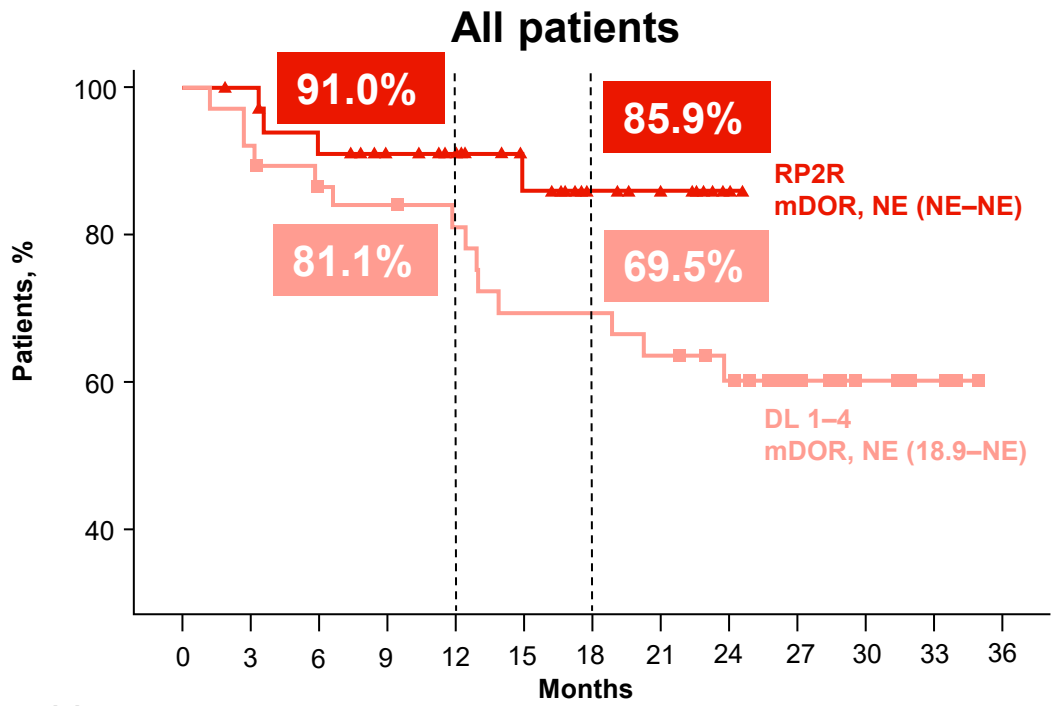
Data cut-off date: March 15, 2024.

[a]EMD defined as ≥1 nonradiated, bone-independent lesion ≥2 cm. [b]Responses were investigator-assessed per IMWG 2016 criteria. Data shown are confirmed responses and calculated in all treated patients. [c]Denotes patients who died. CR, complete response; DL, dose level; EMD, extramedullary disease; IMWG, International Myeloma Working Group; ORR, overall response rate; PR, partial response; RP2R, recommended phase 2 regimen; sCR, stringent complete response; tal, talquetamab; tec, teclistamab; VGPR, very good partial response.

Presented by YC Cohen at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

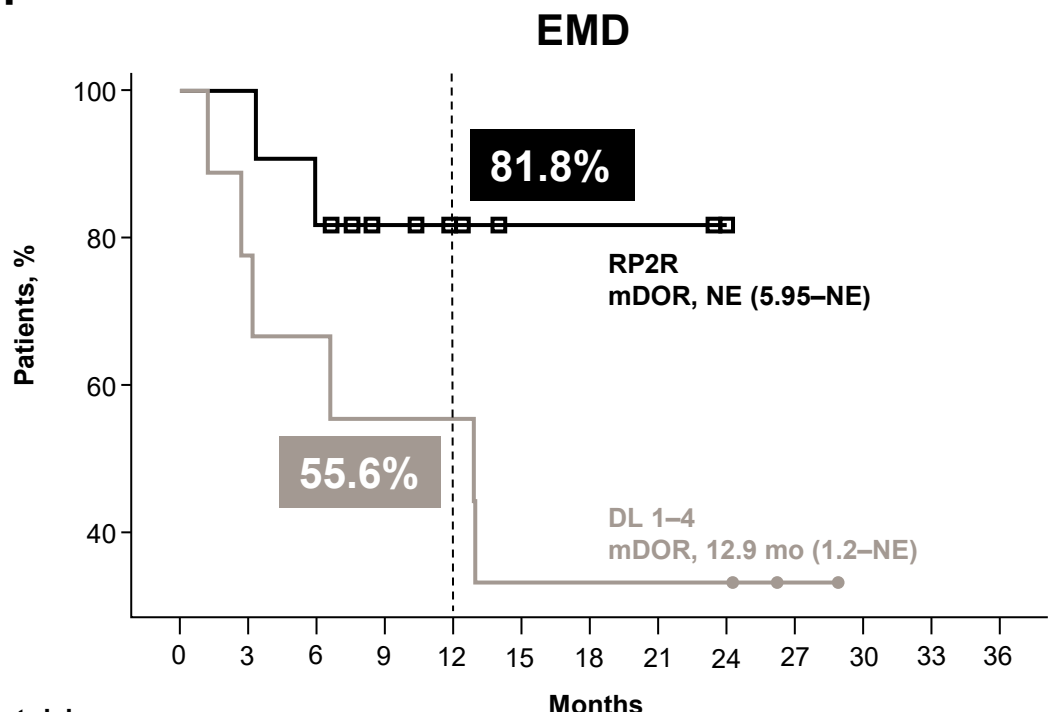
RedirecTT-1 Tal + Tec: Highly Durable Responses, Including in EMD[a]

Duration of response



Patients at risk

DL 1–4	38	35	31	30	28	24	24	22	18	12	5	3	0
RP2R	35	34	30	26	23	17	10	7	2	0	0	0	0



Patients at risk

DL 1–4	9	7	6	5	5	3	3	3	3	1	0	0	0
RP2R	11	11	9	6	5	2	2	2	1	0	0	0	0

18-mo DOR of 85.9% better at RP2R (81.8% 12-mo rate in EMD)

Data cut-off date: March 15, 2024. Median follow-up: 18.2 months (RP2R) and 29.0 months (dose levels 1–4). [a]EMD defined as ≥1 nonradiated, bone-independent lesion ≥2 cm. DL, dose level; EMD, extramedullary disease; mDOR, median duration of response; NE, not evaluable; RP2R, recommended phase 2 regimen; tal, talquetamab; tec, teclistamab.

Presented by YC Cohen at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

RedirecTT-1 Tal + Tec: Findings From >1 Year Follow-Up

- **Tal + tec had a safety profile generally consistent with each agent as monotherapy**
  - Infections were common but new-onset grade ≥3 infections declined at 6 months
  - RP2R safety profile consistent with safety profile observed at all other dose levels
- **Deep and durable responses at the RP2R**
  - ORR of 79.5% (≥CR, 52.3%)
  - 18-month DOR rate of 85.9%, 18-month PFS rate of 69.8%
- **In EMD, best reported ORR and DOR for BsAb-based treatment at the RP2R**
  - ORR of 61.1% (≥CR, 33.3%)
  - 12-month DOR rate of 81.8%, 12-month PFS rate of 52.9%
- **Dual targeting of GPRC5D and BCMA may avoid antigen escape and clonal resistance**

RedirecTT-1, the first study combining 2 BsAbs to achieve dual-antigen targeting, demonstrated deep and durable responses in RRMM, with impressive efficacy in hard-to-treat patients with EMD

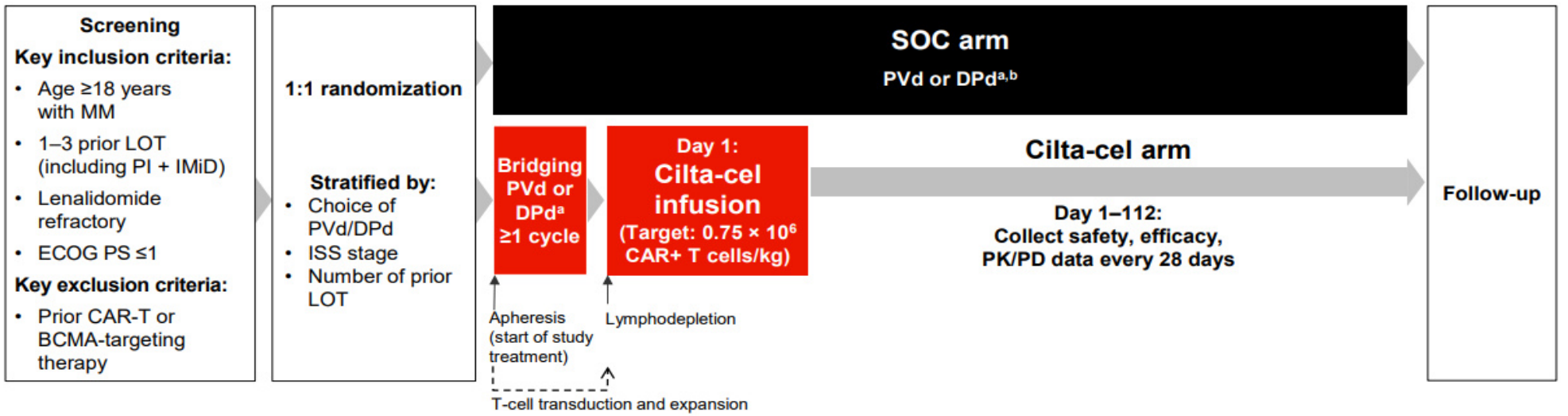
BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CR, complete response; DOR, duration of response; EMD, extramedullary disease; GPRC5D, G protein–coupled receptor family C group 5 member D; ORR, overall response rate; PFS, progression-free survival; RP2R, recommended phase 2 regimen; RRMM, relapsed/refractory multiple myeloma; tal, talquetamab; tec, teclistamab.

Presented by YC Cohen at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

Overall Survival With Ciltacabtagene Autoleucel Versus Standard of Care in Lenalidomide-Refractory Multiple Myeloma: Phase 3 CARTITUDE-4 Study Update

María-Victoria Mateos[1], Jesús San-Miguel[2], Binod Dhakal[3], Cyrille Touzeau[4], Xavier Leleu[5], Niels WCJ van de Donk[6], Surbhi Sidana[7], Albert Oriol[8], Yaël C Cohen[9], Simon J Harrison[10, 11, 12], Hermann Einsele[13], Paolo Corradini[14], Diana Chen[15], Quanlin Li[16], Katherine Li[17], Ana Slaughter[18], Carolina Lonardi[19], Nina Benachour[20], Martin Vogel[21], Nikoletta Lendvai[22], Mythili Koneru[23], Nitin Patel[23], Erika Florendo[23], P Joy Ho[24], Rakesh Popat[25]

CARTITUDE-4: Study Design and Endpoints[1]



Primary endpoint
- PFS[c,d]

Secondary endpoints
- Efficacy: ≥CR, ORR, MRD negativity, OS[d]
- PROs
- Incidence and severity of AEs[e]

CARTITUDE-4:
Baseline Characteristics Generally Balanced Across Arms

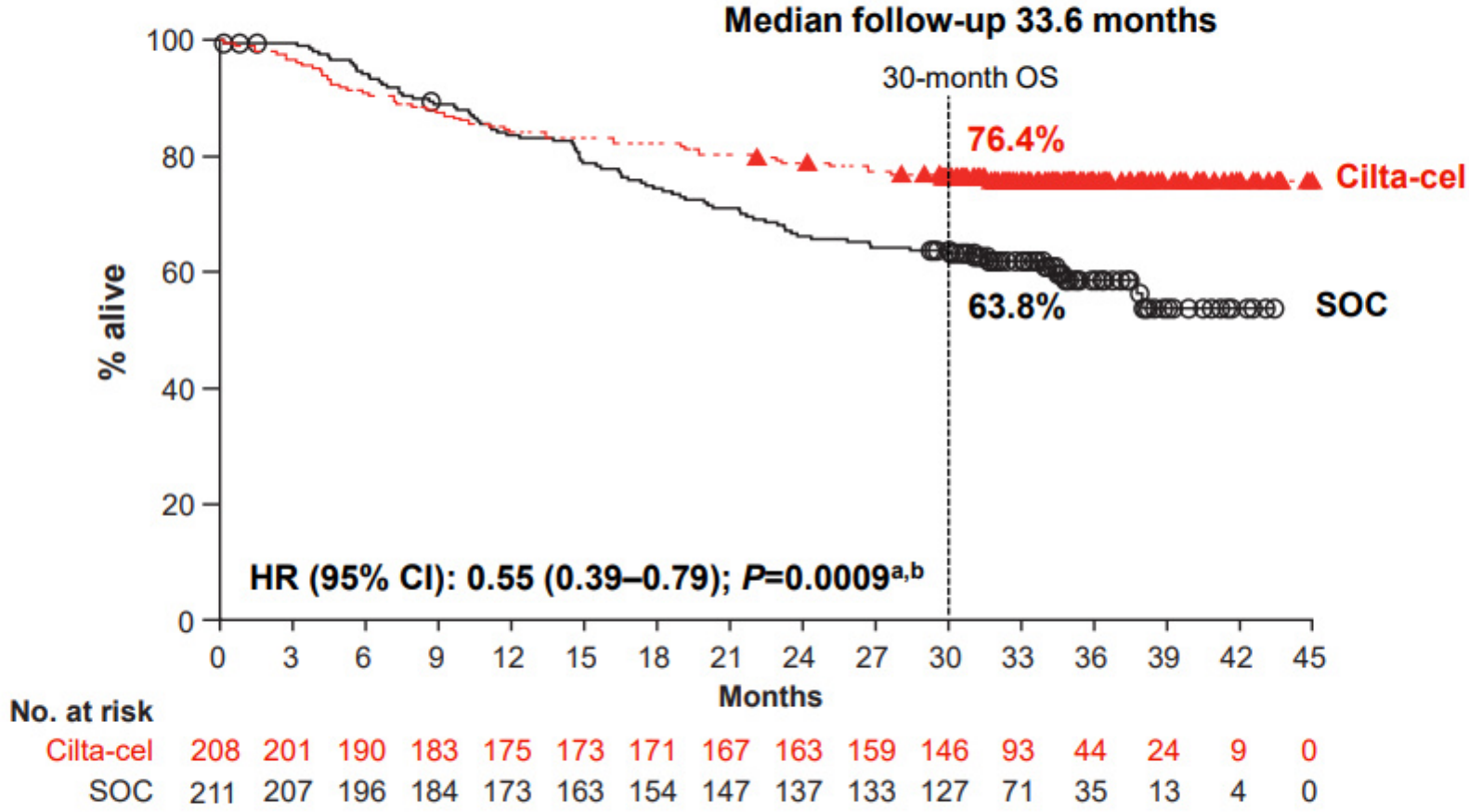
Baseline characteristic	ITT population	
	Cilta-cel (n=208)	SOC (n=211)
Age, median (range), years	61.5 (27–78)	61.0 (35–80)
Male, n (%)	116 (55.8)	124 (58.8)
ISS stage, n (%)		
I	136 (65.4)	132 (62.6)
II	60 (28.8)	65 (30.8)
III	12 (5.8)	14 (6.6)
Presence of soft tissue plasmacytomas,[a] n (%)	44 (21.2)	35 (16.6)
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,[b] n (%)	123 (59.4)	132 (62.9)
del(17p)	49 (23.7)	43 (20.5)
t(14;16)	3 (1.4)	7 (3.3)
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 exposed,[c] n (%)	53 (25.5)	55 (26.1)
Penta-drug exposed,[d] n (%)	14 (6.7)	10 (4.7)
Refractory status, n (%)		
Triple-class refractory[c,e]	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]Including extramedullary and bone-based plasmacytomas with measurable soft tissue component. [b]In 207 (cilta-cel arm) and 210 (SOC arm) patients. [c]Including 1 PI, 1 IMiD, and 1 anti-CD38 monoclonal antibody.
[d]Including ≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 monoclonal antibody. [e]2 patients (cilta-cel arm) and 1 patient (SOC arm) were penta-drug refractory.
Cilta-cel, ciltacabtagene autoleucel; IMiD, immunomodulatory drug; ISS, International Staging System; ITT, intent-to-treat; LOT, line of therapy; PI, proteasome inhibitor; SOC, standard of care.

Presented by M-V Mateos at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

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

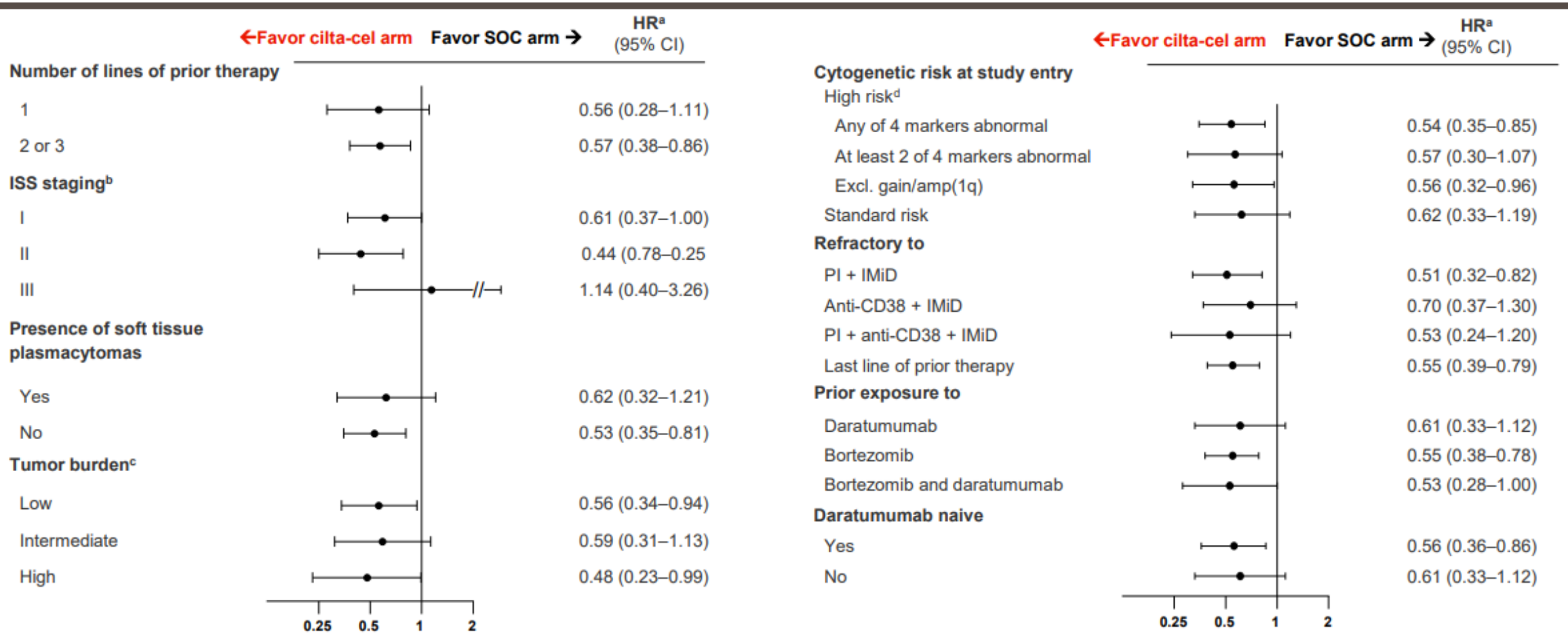


First CAR-T to demonstrate overall survival benefit in multiple myeloma

[a]Log-rank test. *P*-value, 0.0009, crossed the prespecified boundary of 0.0108 as implemented by the Kim-DeMets spending function with parameter=2. [b]Hazard ratio and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable.
CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; OS, overall survival; SOC, standard of care.

Presented by M-V Mateos at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

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

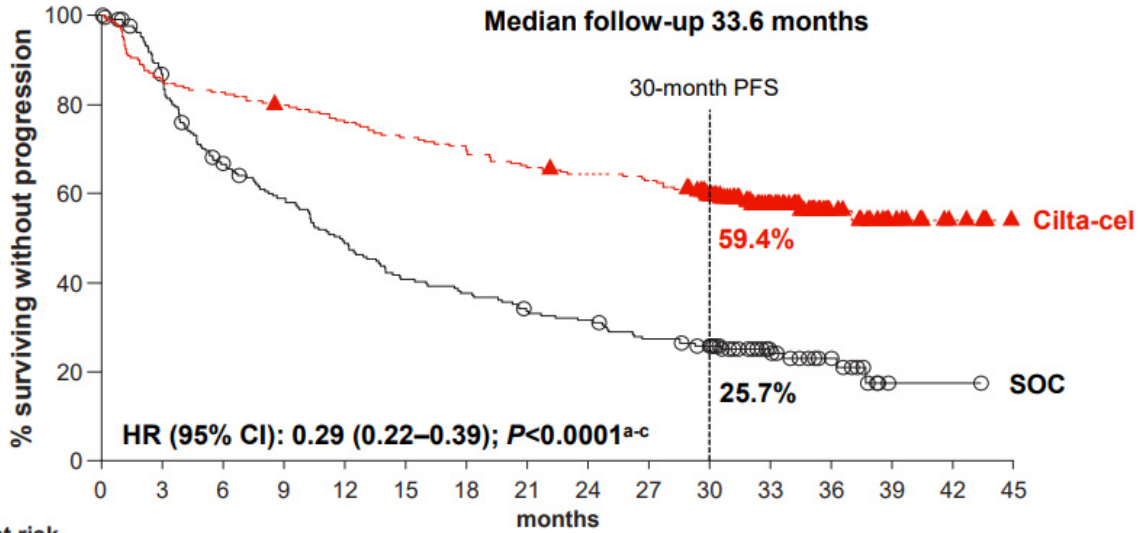


Consistent reduction in risk of death across prespecified subgroups[e]

[a]HR and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable. HR <1 indicates an advantage for the cilta-cel arm. [b]Based on serum β_2-microglobulin and albumin. [c]Low tumor burden defined as meeting all following parameters (as applicable): bone marrow % plasma cell <50%, serum M-protein <3 g/dL, serum free light chain <3000 mg/L; high tumor burden defined as meeting any of the following parameters: bone marrow % plasma cell ≥80%, serum M-protein ≥5 g/dL, serum free light chain ≥5000 mg/L; intermediate tumor burden did not fit either criteria of high or low tumor burden. [d]Positive for del(17p), t(14;16), t(4;14), and/or gain/amp(1q) by fluorescence in situ hybridization testing. Protocol-defined high-risk cytogenetics refers to "Any of 4 markers abnormal". [e]Except ISS stage III, which had n=12 in cilta-cel arm and n=14 in SOC arm.
Cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; IMiD, immunomodulatory drug; ISS, International Staging System; OS, overall survival; PI, proteasome inhibitor; SOC, standard of care.

Presented by M-V Mateos at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

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



No. at risk																
Cilta-cel	208	177	172	165	157	150	145	136	132	129	111	65	29	13	5	0
SOC	211	176	133	116	96	80	74	65	61	52	47	25	12	1	1	0

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

[a]Constant piecewise weighted log-rank test. [b]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.
[c]Nominal *P* value.
Cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; mPFS, median progression-free survival; PFS, progression-free survival; SOC, standard of care.

Presented by M-V Mateos at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

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)

Long-Term CARTITUDE-4 Update (34 Months): Conclusions

- Cilta-cel is the first CAR-T cell therapy to show significant OS benefit in MM
  - 45% reduction in the risk of death with cilta-cel vs SOC in patients with lenalidomide-refractory MM after 1–3 prior LOT
  - Consistent OS benefit across subgroups
- Median OS and PFS were not reached with cilta-cel
- QoL was significantly improved with cilta-cel vs SOC
- Safety profile was consistent with previous analysis

A one-time cilta-cel infusion significantly prolonged OS and improved QoL

A Phase 1 Study of P-BCMA-ALLO1, a Non-viral, Allogeneic BCMA Directed CAR-T in Relapsed/Refractory Multiple Myeloma (RRMM)

Bhagirathbhai Dholaria, Mehmet Kocoglu, Andrew Kin, Aravind Ramakrishnan, Leyla Shune, Sidhartha Ganguly, Jose Cruz, Christopher Strouse, Ehsan Malek, Edward Faber, Katherine McArthur, Joanne McCaigue, Samuel DePrimo, Christopher Martin, Sabrina Haag, Jeff D Eskew, Hamid Namini, Ellen Christie, Rajesh Belani, Syed Rizvi, Stacey Cranert, Julia Coronella, Devon J. Shedlock, Caitlin Costello

International Myeloma Society (IMS) 21st Annual Meeting and Exposition 2024

Presented by:

Bhagirathbhai Dholaria, MD

Associate Professor of Medicine

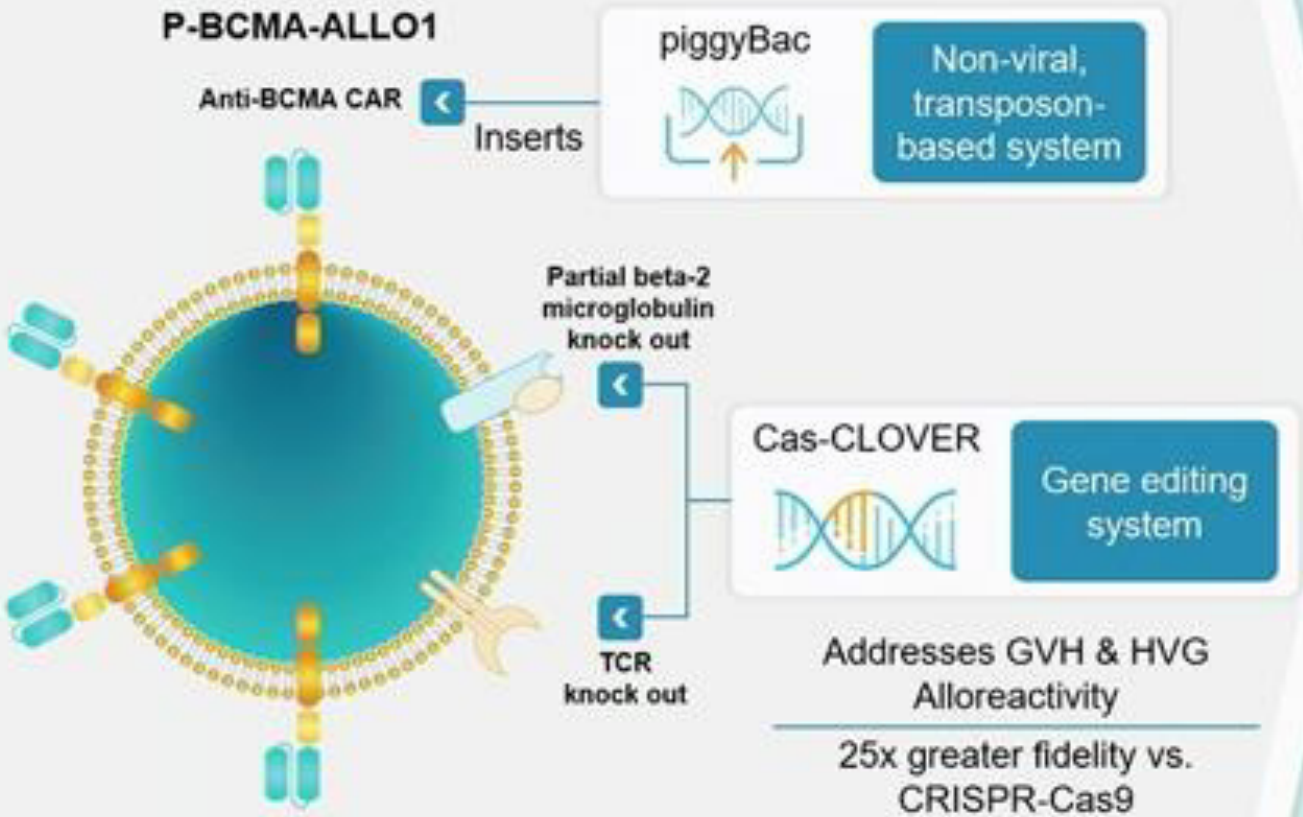
Malignant Hematology & Stem Cell Transplantation

Vanderbilt University Medical Center, Nashville, TN, USA

VANDERBILT UNIVERSITY

MEDICAL CENTER

P-BCMA-ALLO1 is a non-viral, stem cell memory T cell-rich, allogeneic CAR T that enables cellular expansion and anti-tumor activity with enhanced scalability



Proprietary technologies used to create P-BCMA-ALLO1 with high percentage of stem cell memory T cell (T_{scm})

- T_{scm} have a less differentiated phenotype, which is associated with prolonged persistence and improved antitumor reactivity and expansion

Drug resistance gene permits positive selection

- ~100% of T cells in final product express the CAR

Incorporates proprietary safety switch

- Rapid, dose-dependent elimination of engineered T cells if necessary in case of severe toxicity

ARM C: Baseline characteristics & prior therapy

Heavily pretreated patients, most with prior anti-BCMA exposure

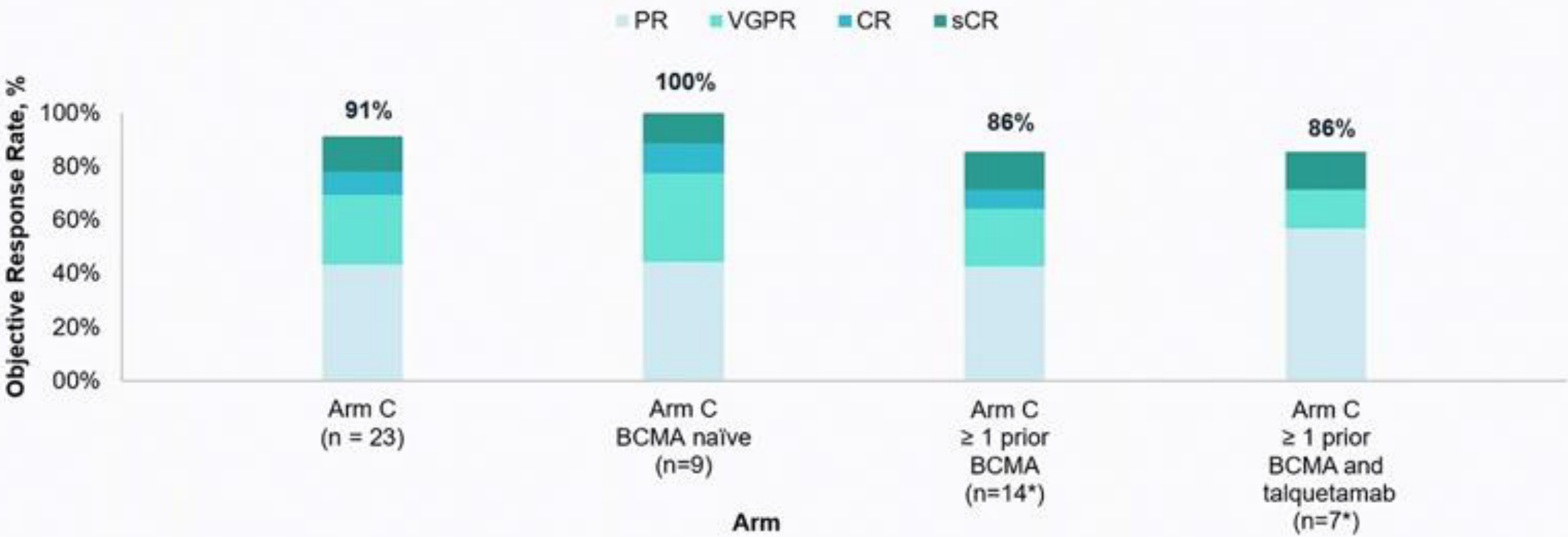
Demographics/Characteristics	Total (n=21)
Median age, y (min, max)	61 (39, 76)
Female/male, n (%)	11 (52) / 10 (48)
Time since diagnosis, y, median (min, max)	5.1 (1.0 15.1)
High Risk Cytogenetics, n (%)**	**13 (62)**
ECOG (Baseline) PS, 0 /1 n (%)	8 (38) / 13 (62)
Extramedullary disease, n (%)	**8 (38)**
Race, n (%)	White, 13 (62) **Minorities, 8 (38)***

Prior Therapy Exposure	Total (n=21)
# of prior regimens, median (min, max)	**6 (2, 14)**
Prior anti-BCMA/talquetamab therapy, n (%)	**13 (62)**
Prior anti-BCMA bispecific only	3 (14)
Prior BCMA auto CAR-T only	2 (10)
Prior BCMA auto CAR-T and ADC	1 (5)
Prior anti-BCMA bispecific and BCMA auto CAR-T	6 (29)
Prior anti-BCMA bispecific, BCMA auto CAR-T, and ADC	1 (5)
Prior talquetamab and BCMA	6 (29)
Bridging therapy	**0 (0)**
Prior ASCT	**14 (67)**

Study population includes heavily pre-treated & high-risk patients, many of whom received prior anti-BCMA/talq therapy

2 Re-Treatment subjects not included on this slide to avoid duplication of demographic information

P-BCMA-ALLO1 is highly clinically active in both BCMA naïve and BCMA exposed patients



- ORR= sCR, CR, VGPR or PR, including confirmed and unconfirmed responses. Evaluable patients: Obtained first response assessment by IMWG m-protein criteria or PD/death and completed Week 4 visit
- Arm: C = LD – cy 750 mg/m², flu 30mg/m²
- All dosed Cohort 2 = Range 2.0 to < 6.0 × 10^6 cells/kg

Note: 2 Re-Treatment subjects included in arm C. * Includes 1 retreatment subject

P-BCMA-ALLO1 Phase 1 interim data summary

Rapid, accessible and "off the-shelf" investigational allogeneic CAR-T to treat patients without waiting

- **100% of ITT population** underwent LD and received P-BCMA-ALLO1, with several treated in outpatient setting
  - No invasive apheresis and manufacturing wait time
  - No anti-myeloma bridging therapy

Compelling safety profile in a highly refractory and heavily pretreated patient population

- No steroid or tocilizumab prophylaxis
- **No DLTs, no grade ≥3 CRS or ICANS, no GvHD, no HLH/MAS, no Parkinsonism or cranial neuropathies**
- **Low CRS (27%, all events ≤ Grade 2) and low infection rates (13% G3+ events)**
- Rapid cytopenia recovery to grade ≤2 **occurred in 82% of** patients by day 30 after P-BCMA-ALLO1 infusion
- Further characterization of safety profile is ongoing

Exceptional clinical activity in a heavily pretreated population, including in BCMA-exposed patients

- Diverse patient population including 69% with high-risk cytogenetics, patients with extramedullary disease and those who have failed BCMA as well as GPRC5D directed therapies
- **>90% ORR in arm C (cyclophosphamide 750 mg/m²)**
- **Arm C: 100% ORR in BCMA naïve patients; 86% ORR in prior BCMA/talq-exposed patients**

Study is ongoing, currently enrolling patients in Phase Ib utilizing optimized Arm C LD (NCT04960579)

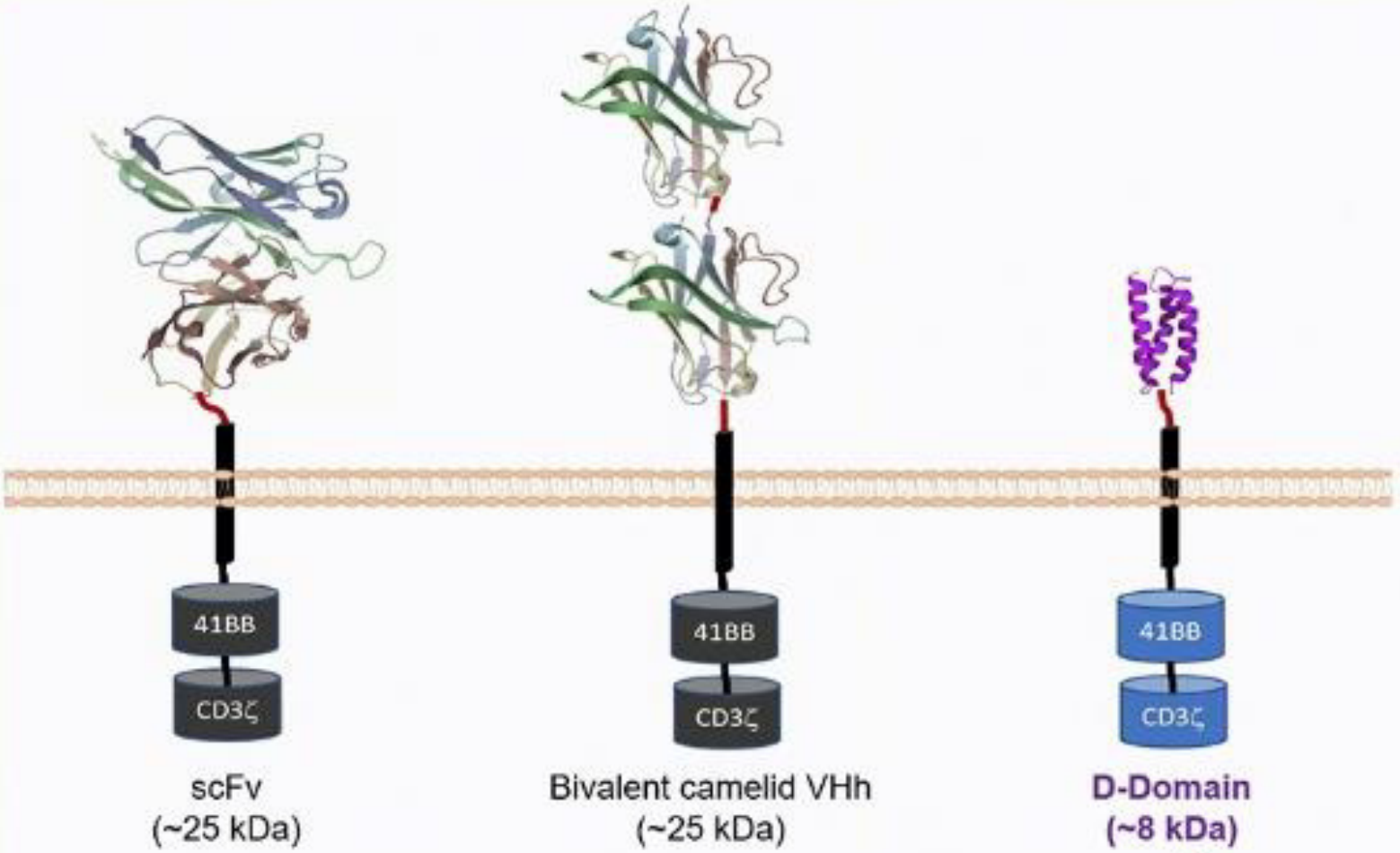
P-BCMA-ALLO1 received RMAT designation by the FDA recently, as well as ODD previously.

Phase 1 Study Of Anito-cel (CART-ddBCMA) For The Treatment Of Patients With Relapsed And/Or Refractory Multiple Myeloma: Results From At Least 1-year Follow-up In All Patients

Matthew Frigault, MD, MS, Jacalyn Rosenblatt, MD, ***Binod Dhakal, MD, MS****, Noopur Raje, MD, Daniella Cook, BS, Mahmoud R. Gaballa, MD, Estelle Emmanuel-Alejandro, Danielle Nissen, Kamalika Banerjee, Anand Rotte, PhD, Christopher R. Heery, MD, David Avigan, MD, Andrzej Jakubowiak, MD, PhD and Michael R. Bishop, MD*

Anitocabtagene autoleucel (anito-cel/CART-ddBCMA)

Autologous BCMA-directed CAR T-cell therapy using a novel, D-Domain binder[1]



D-Domain Attributes:
Non-Antibody Derived Synthetic Protein[1,2]

Size	**Small D-Domain construct facilitates high transduction efficiency, CAR positivity, and CAR density on the T-cell surface[2-4]**
Stability	**Rapid D-Domain folding, lack of disulfide bonds, and a hydrophobic core enables D-Domain CAR stability[5,6]**
Structure	**Due to small size and compact structure, D-Domain CARs have a low risk of tonic signaling[6] and potentially more efficient Multiple Myeloma cell killing**

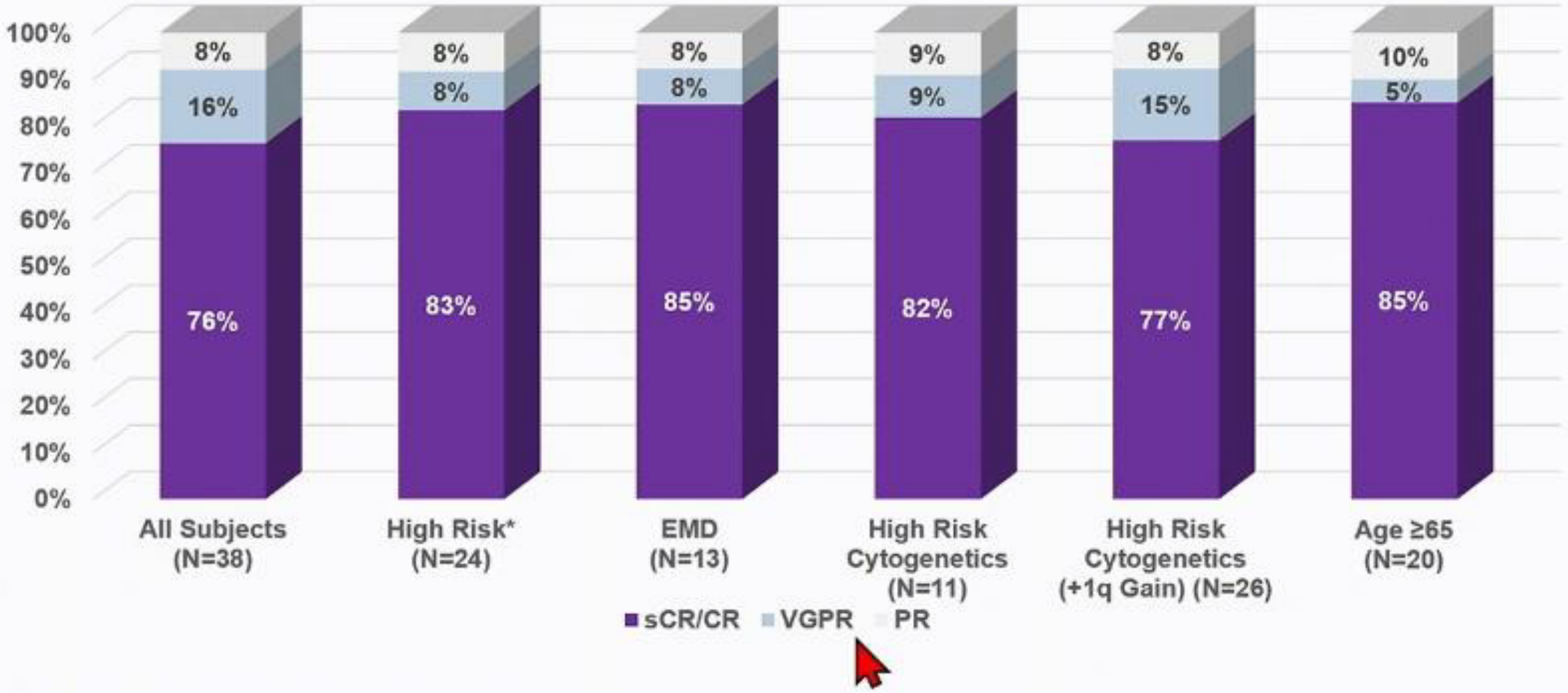
[1]Rotte, et al. *Immuno-Oncology Insights* 2022; 3(1), 13–24; [2]Frigault, et al. *Blood Adv.* 2023; 7(5):768-777; [3]Cante-Barrett, et al. *BMC Res. Notes* 2016; 9:13; [4]Buonato, et al. *Mol. Cancer Ther.* 2022; 21(7):1171-1183; [5]Zhu, et al. *Proc. Nat. Acad. Sci.* 2003; 100(26): 15486-15491; [6]Qin, et al. *Mol. Ther.* 2019; 27(7): 1262-1274.

Anito-cel Phase 1 Results: Patient Demographics

Characteristics	Dose Level 1 100 million CAR-T (n=32)	Dose Level 2 300 million CAR-T (n=6)	Total (n=38)
Age, median (min - max)	66 (44 - 76)	60 (52 - 65)	66 (44 - 76)
Gender	18 Male (56%) 14 Female (44%)	5 Male (83%) 1 Female (17%)	23 Male (61%) 15 Female (39%)
ECOG PS[a]			
0	9/32 (28%)	3/6 (50%)	12/38 (32%)
1	23/32 (72%)	3/6 (50%)	26/38 (68%)
High Risk Prognostic Feature	18/32 (56%)	6/6 (100%)	24/38 (63%)
BMPC ≥60%	6/32 (19%)	3/6 (50%)	9/38 (24%)
ISS Stage III (B2M ≥ 5.5)	5/32 (16%)	2/6 (33%)	7/38 (18%)
Extra-medullary disease[b]	10/32 (31%)	3/6 (50%)	13/38 (34%)
High Risk Cytogenetics[c] Inclusive of 1q Gain	21/32 (66%)	5/6 (83%)	26/38 (64%)
High Risk Cytogenetics[c]	9/32 (28%)	2/6 (33%)	11/38 (29%)
Prior Lines of Therapy, Median (min - max)	5 (3 - 7)	4 (3 - 16)	4 (3 - 16)
Triple refractory	32/32 (100%)	6/6 (100%)	38/38 (100%)
Penta refractory	21/32 (66%)	5/6 (83%)	26/38 (68%)
Refractory to last line of therapy	28/32 (88%)	6/6 (100%)	34/38 (89%)
Time since diagnosis, median (min-max)	6.5 years (1.5 – 14.9 years)	6.9 years (1.7 – 11.0 years)	6.5 years (1.5 – 14.9 years)
Bridging therapy	20/32 (63%)	6/6 (100%)	26/38 (68%)
Previous ASCT	25/32 (78%)	4/6 (67%)	29/38 (76%)

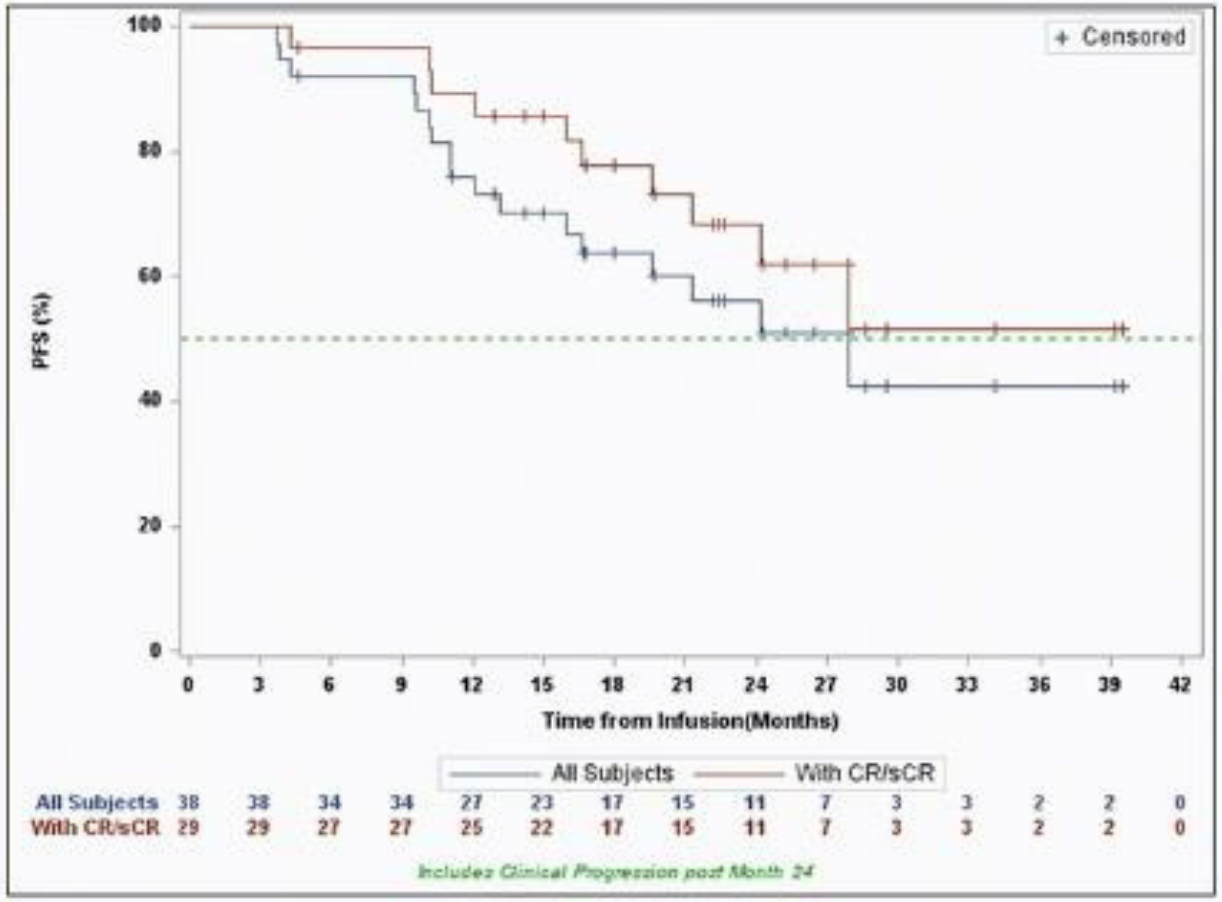
Note: As of October 15, 2023; a) Eastern Cooperative Oncology Group Performance Status Scale; b) EMD is a form of Multiple Myeloma characterized by the presence of a non-bone based plasmacytoma; c) Defined as the presence of Del 17p, t(14;16), t(4;14).

Anito-cel Phase 1 Results: Best Overall Response



Anito-cel Phase 1 Results: PFS for All Patients, CR/sCR Patients

Median Follow-Up: All Patients 26.5-mo. [14-44]; CR/sCR Patients 26.5-mo. [15-44]



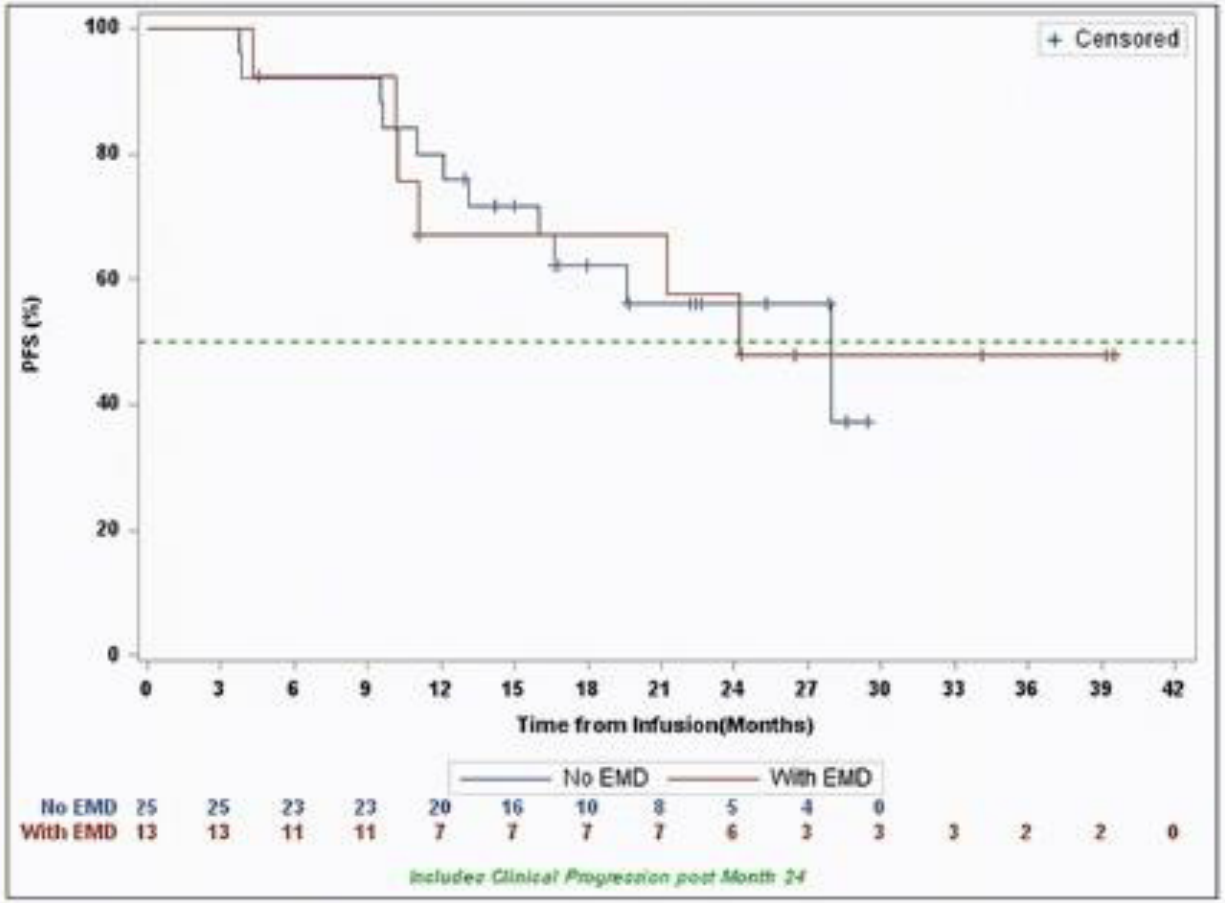
	Time (months)	PFS Estimate (%)	95% Confidence Interval (%)
All Patients (n = 38)	6	92.1	77.5, 97.4
	12	75.9	58.7, 86.6
	18	63.7	45.7, 77.2
	24	56.0	37.3, 71.1

- **Median PFS not reached for all patients (n=38)**
- **Median PFS not reached for CR/sCR patients (n=29, 76%)**
- **89% (n=25/28) of evaluable* patients MRD negative at minimum of 10^{-5} sensitivity**

Note: Data cut-off October 15, 2023; * Evaluable patients had identifiable malignant clone in the baseline bone marrow aspirate

Anito-cel Phase 1 Results: PFS for Patients With or Without EMD

Median Follow-Up: EMD Patients ~33-mo. [14-44]; Non-EMD Patients ~25-mo. [15-40]



	Time (months)	PFS Estimate (%)	95% Confidence Interval (%)
With EMD (n = 13)	6	92.3	56.6, 98.9
	12	67.1	34.2, 86.2
	18	67.1	34.2, 86.2
	24	57.5	25.7, 79.9

- **Median PFS not reached for patients with EMD (n=13)**
- **Median PFS not reached for Non-EMD patients (n=25)**

Note: Data cut-off October 15, 2023

Anito-cel Phase 1 Results: Safety

- No delayed neurotoxicities, no Guillain-Barré syndrome, no cranial nerve palsies, and no Parkinsonian-like syndromes in the entire population through the follow-up period
- One Grade 5 AE post study treatment (unrelated cardiac arrest due to non-study drug overdose)
- No change in safety profile as previously presented

CAR-T-associated AEs Per ASTCT criteria	100 million (n=32)		300 million (n=6)	
Cytokine Release Syndrome (CRS)	**Grade 1/2**	**Grade 3**	**Grade 1/2**	**Grade 3**
	30 (94%)	**0**	**5 (83%)**	**1 (17%)**
Median onset (min-max)*	2 days (1-12 days)		2 days (1-2 days)	
Median duration (min-max)	6 days (1-10 days)		5 days (3-9 days)	
Neurotoxicity (ICANs)	**Grade 1/2**	**Grade 3**	**Grade 1/2**	**Grade 3**
	5 (16%)	**1 (3%)**	**0**	**1 (17%)**
Median onset (min-max)*	4.5 days (3-6 days)		7 days	
Median duration (min-max)	3.5 days (1 - 9 days)		17 days	
Toxicity Management				
Tocilizumab	27 (84%)		5 (83%)	
Dexamethasone	20 (63%)		2 (33%)	

Grade 3/4 AEs (non-CRS/ICANS) ≥5% after cell infusion (n=38)	
Hematologic	
Neutrophil count decreased	31 (81.6%)
Anemia	22 (57.9%)
Thrombocytopenia	16 (42.1%)
Lymphocyte count decreased	15 (39.5%)
White blood cell count decreased	7 (18.4%)
Febrile Neutropenia	5 (13.2%)
Non-hematologic	
Hypertension	3 (7.9%)
AST[a] increased	2 (5.3%)
Cellulitis	2 (5.3%)
Hypokalemia	2 (5.3%)
Hyponatraemia	2 (5.3%)
Hypophosphatemia	2 (5.3%)
Lung Infection	2 (5.3%)
Pain in extremity	2 (5.3%)
Sepsis[b]	2 (5.3%)

Note: Median duration numbers updated due to ongoing data review; a) Aspartate Aminotransferase Test; b) Grouped category for sepsis

Anito-cel Phase 1 Results: Safety

- No delayed neurotoxicities, no Guillain-Barré syndrome, no cranial nerve palsies, and no Parkinsonian-like syndromes in the entire population through the follow-up period
- One Grade 5 AE post study treatment (unrelated cardiac arrest due to non-study drug overdose)
- No change in safety profile as previously presented

CAR-T-associated AEs Per ASTCT criteria	100 million (n=32)		300 million (n=6)	
Cytokine Release Syndrome (CRS)	**Grade 1/2**	**Grade 3**	**Grade 1/2**	**Grade 3**
	30 (94%)	**0**	**5 (83%)**	**1 (17%)**
Median onset (min-max)*	2 days (1-12 days)		2 days (1-2 days)	
Median duration (min-max)	6 days (1-10 days)		5 days (3-9 days)	
Neurotoxicity (ICANs)	**Grade 1/2**	**Grade 3**	**Grade 1/2**	**Grade 3**
	5 (16%)	**1 (3%)**	**0**	**1 (17%)**
Median onset (min-max)*	4.5 days (3-6 days)		7 days	
Median duration (min-max)	3.5 days (1 - 9 days)		17 days	
Toxicity Management				
Tocilizumab	27 (84%)		5 (83%)	
Dexamethasone	20 (63%)		2 (33%)	

Grade 3/4 AEs (non-CRS/ICANS) ≥5% after cell infusion (n=38)	
Hematologic	
Neutrophil count decreased	31 (81.6%)
Anemia	22 (57.9%)
Thrombocytopenia	16 (42.1%)
Lymphocyte count decreased	15 (39.5%)
White blood cell count decreased	7 (18.4%)
Febrile Neutropenia	5 (13.2%)
Non-hematologic	
Hypertension	3 (7.9%)
AST[a] increased	2 (5.3%)
Cellulitis	2 (5.3%)
Hypokalemia	2 (5.3%)
Hyponatraemia	2 (5.3%)
Hypophosphatemia	2 (5.3%)
Lung Infection	2 (5.3%)
Pain in extremity	2 (5.3%)
Sepsis[b]	2 (5.3%)

Note: Median duration numbers updated due to ongoing data review; a) Aspartate Aminotransferase Test; b) Grouped category for sepsis

Anito-cel Phase 1 Results: Conclusions

- **Anito-cel utilizes a novel, synthetic, compact and stable D-Domain binder**
  - D-Domain facilitates high CAR surface expression, low risk of tonic signaling
  - Recommended Phase 2 Dose selected as 115 ±10 million CAR+ T cells
- **CR/sCR rate 76%; 100% ORR per IMWG**
  - CR/sCR rate >77% in all sub-groups including high-risk (EMD, high-risk cytogenetics, age ≥65)
  - 89% of MRD evaluable patients (n=25/28) were MRD negative at 10^{-5} or lower
- **Median PFS, DOR, and OS not reached at 2 years with a median follow-up of 26.5 months**
  - Anito-cel continues to demonstrate deep and durable efficacy, including in high-risk patient sub-groups
- **At 2 years of follow-up (median 26.5 months), manageable safety profile**
  - No grade ≥3 CRS and 1 case of Grade 3 ICANS at RP2D. All events resolved without sequelae with routine management
  - No delayed neurotoxicity, no cranial nerve palsy, no Parkinsonian symptoms, no Guillain-Barré syndrome

Anito-cel is being co-developed with Kite's global cell therapy leadership

iMMagine-1 (NCT05396885) is the pivotal Phase 2 trial evaluating anito-cel in patients with RRMM and ≥3 prior LoT including a proteosome inhibitor, an iMiD, and an anti-CD38 monoclonal antibody

iMMagine-3 (NCT06413498) is a global, Phase 3 trial comparing anito-cel to standard of care therapy in patients with RRMM after 1-3 prior LoT, including an anti-CD38 monoclonal antibody and an iMiD

Muito obrigado !