

Updated results of ciltacabtagene autoleucel (cilta-cel), a B-cell maturation antigen (BCMA)–directed chimeric antigen receptor T (CAR-T) cell therapy, in relapsed/refractory multiple myeloma (RRMM)

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INTRODUCTION

- CARTITUDE-1 (NCT03548207) is a phase 1b/2 study evaluating cilta-cel, a chimeric antigen receptor (CAR) T cell therapy with 2 B-cell maturation antigen (BCMA)–targeting single-domain antibodies, in patients with relapsed/refractory multiple myeloma (RRMM) who have been heavily pretreated¹
- At a median follow-up of 12.4 months after cilta-cel treatment, the overall response rate (ORR) was 97% with a stringent complete response (sCR) rate of 67%; overall 12-month progression-free survival (PFS) and overall survival (OS) rates were 77% and 89%, respectively

OBJECTIVE

To present updated results from CARTITUDE-1 in patients with longer follow-up (median, 18 months)

METHODS

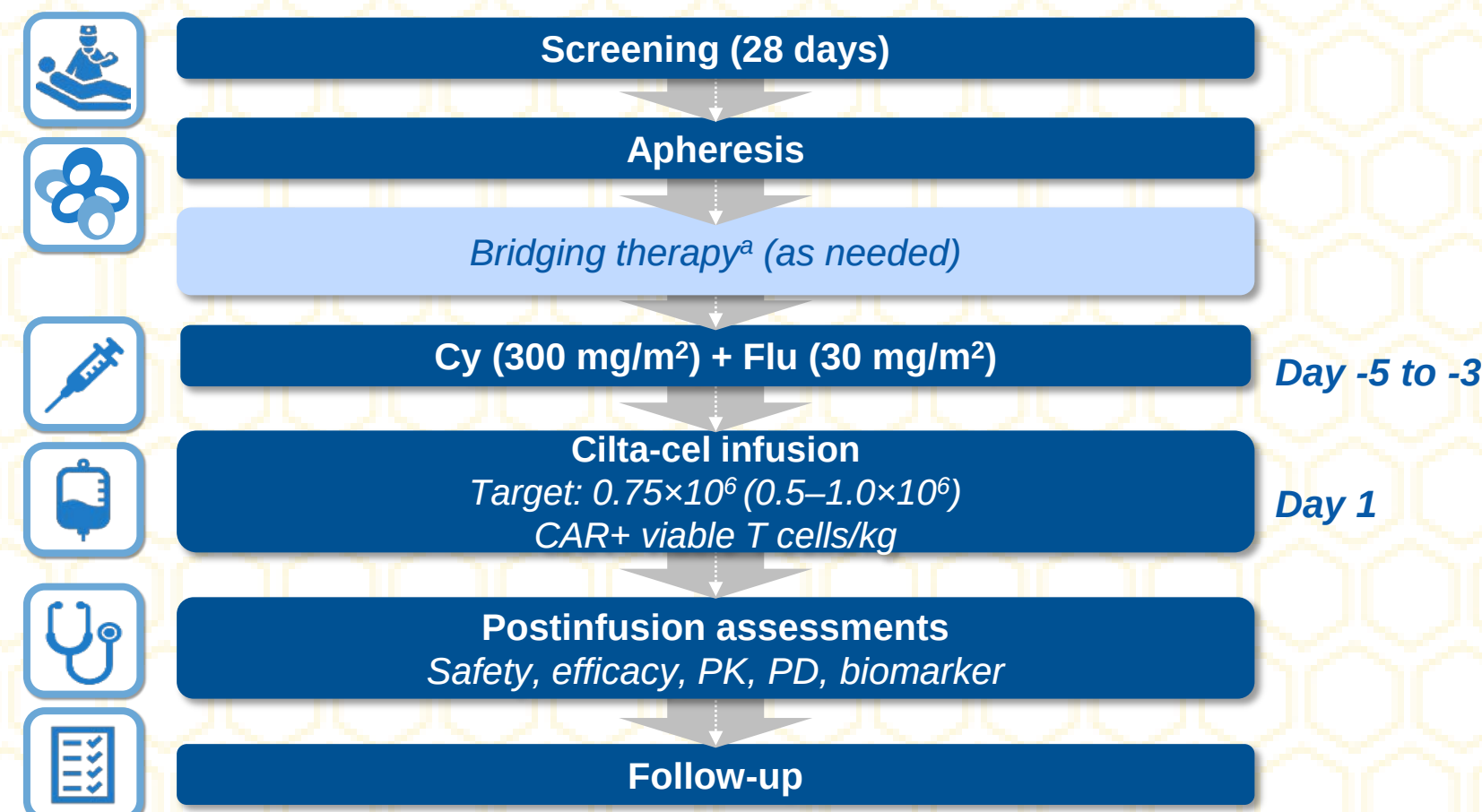
Study Design

- The CARTITUDE-1 study design is shown in **Figure 1**
- Median administered dose: 0.71×10^6 (0.51 – 0.95×10^6) CAR+ viable T cells/kg

Key Eligibility Criteria

- Progressive MM per International Myeloma Working Group (IMWG) criteria
- ≥ 3 prior therapies or double refractory to a proteasome inhibitor (PI) and immunomodulatory drug (IMiD) and have received a PI, IMiD, and anti-CD38 antibody
- Measurable disease
- Eastern Cooperative Oncology Group performance status ≤ 1

Figure 1. Study Design



^aTreatment with previously used agent resulting in at least stable disease. 11 Feb 2021 data cut-off. CAR, chimeric antigen receptor; Cy, cyclophosphamide; Flu, fludarabine; PD, pharmacodynamics; PK, pharmacokinetics.

RESULTS

Patients

- A total of 97 patients received cilta-cel infusion; 76 were ongoing at the time of data cut-off
- 73 patients received bridging therapy between apheresis and cilta-cel infusion
- Median turnaround time (time from receipt to release of product) for cilta-cel was 29 days (range, 23–64)
- No patient discontinued due to manufacturing failure
- 1 patient received retreatment with cilta-cel
- 21 patients died during the study: 10 were due to progressive disease, 6 due to treatment-related adverse events (AEs) as assessed by the study investigator, and 5 were due to AEs unrelated to treatment
- Baseline characteristics are shown in **Table 1**

Table 1. Baseline Characteristics

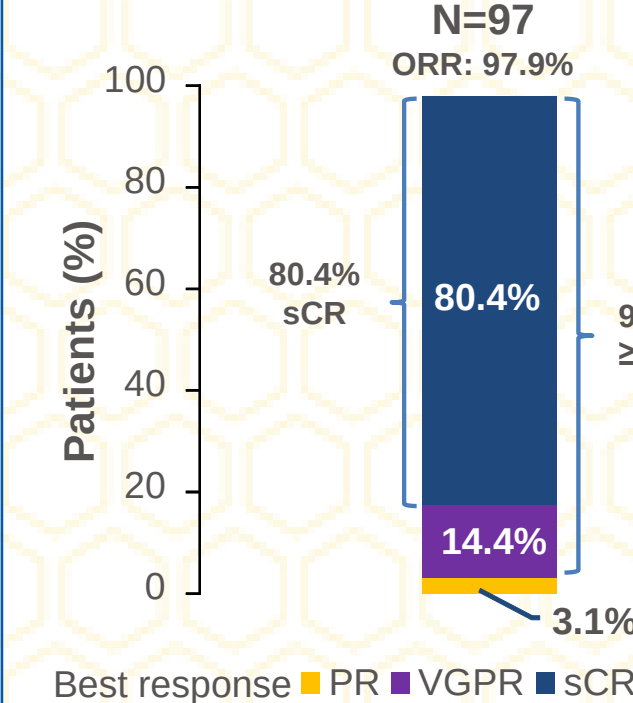
Characteristic	
Age, years, median (range)	61.0 (43–78)
Male, n (%)	57 (58.8)
Black/African American, n (%)	17 (17.5)
All plasmacytomas, ^a n (%)	19 (19.6)
Extramedullary plasmacytomas, n (%)	13 (13.4)
Bone-based plasmacytomas, n (%)	6 (6.2)
Bone-marrow plasma cells $\geq 60\%$, n (%)	21 (21.9)
Years since diagnosis, median (range)	5.9 (1.6–18.2)
High-risk cytogenetic profile, n (%)	23 (23.7)
del17p	19 (19.6)
t(14;16)	2 (2.1)
t(4;14)	3 (3.1)
Tumour BCMA expression $\geq 50\%$, n (%)	57 (91.9) ^b
Prior lines of therapy, median (range)	6.0 (3–18)
Prior lines of therapy, n (%)	
3	17 (17.5)
4	16 (16.5)
≥ 5	64 (66.0)
Previous stem-cell transplantation, n (%)	
Autologous	87 (89.7)
Allogeneic	8 (8.2)
Triple-class exposed, ^c n (%)	97 (100)
Penta-drug exposed, ^d n (%)	81 (83.5)
Triple-class refractory ^c	85 (87.6)
Penta-drug refractory ^d	41 (42.3)
Refractory status, n (%)	
Carfilzomib	63 (64.9)
Pomalidomide	81 (83.5)
Anti-CD38 antibody	96 (99.0)
Refractory to last line of therapy, n (%)	96 (99.0)

^aAll plasmacytomas include extramedullary and bone-based plasmacytomas; ^bDenominator n=62, the number of evaluable samples; BCMA expression detected in all evaluable samples; ^cAt least 1 PI, at least 1 IMiD, and 1 anti-CD38 antibody; ^dAt least 2 PIs, at least 2 IMiDs, and 1 anti-CD38 antibody. BCMA, B-cell maturation antigen; IMiD, immunomodulatory drug; PI, proteasome inhibitor.

Efficacy

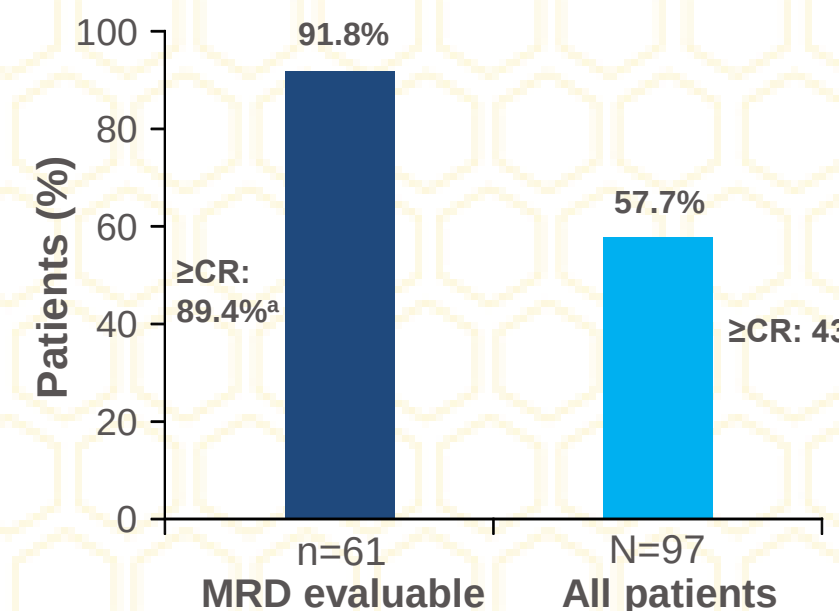
- The ORR was 97.9% (**Figure 2**)
- Median time to first response was 1 month (range, 0.9–10.7), and best response was 2.6 months (range, 0.9–15.2); median time to complete response or better ($\geq$ CR) was 2.6 months (range, 0.9–15.2)
- Duration of response was 21.8 months (95% CI, 21.8–not estimable)
 - Estimated 73% of responders have not progressed or died at 12 months
 - Median duration of response not reached in patients with sCR
- Response rates were comparable (range, 95%–100%) across different subgroups (eg, number of prior lines of therapy, refractoriness, extramedullary plasmacytomas, and cytogenetic risk)
- 91.8% of minimal residual disease (MRD)–evaluable patients and 57.7% of all patients achieved MRD negativity at 10^{-5} threshold (**Figure 3**)
- Median time to MRD 10^{-5} negativity was 1 month (range, 0.8–7.7)
- The 18-month PFS rate in all patients was 66.0% (95% CI, 54.9%–75.0%), and 75.9% (95% CI, 63.6%–84.5%) in those with sCR (**Figure 4**)
- The 18-month OS rate in all patients was 80.9% (95% CI, 71.4%–87.6%)

Figure 2. Overall Response Rate



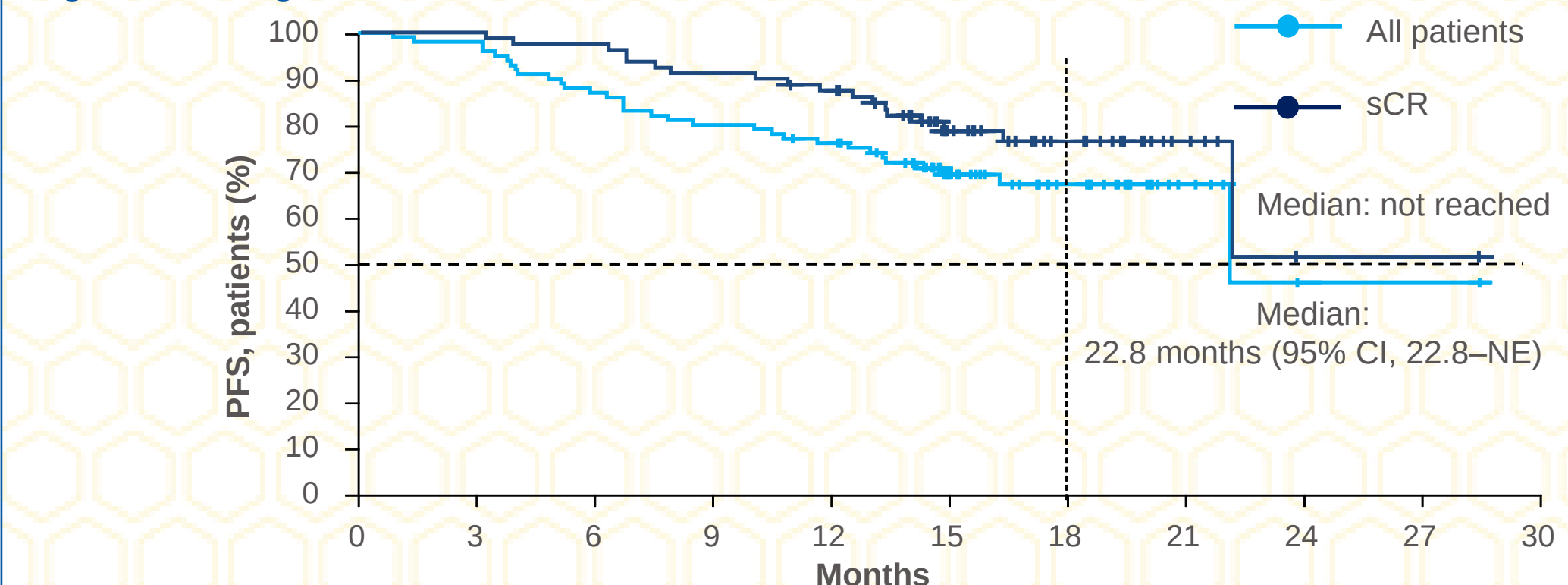
ORR assessed by independent review committee. CR, complete response; ORR, overall response rate; sCR, stringent complete response; VGPR, very good partial response.

Figure 3. MRD Negativity at 10^{-5}



*Denominator n=47; evaluable MRD sample within 3 months of achieving CR/sCR until death/progression/subsequent therapy; MRD was assessed in evaluable samples (ie, patients with identifiable clone at baseline and sufficient cells for testing at 10^{-5} threshold in post treatment samples) by next-generation sequencing (clonoSEQ; Adaptive Biotechnologies) in all treated patients at Day 28, and at 6, 12, 18, and 24 months regardless of the status of disease measured in blood or urine. CR, complete response; MRD, minimal residual disease; sCR, stringent complete response.

Figure 4. Progression-Free Survival



Number at risk		0	3	6	9	12	15	18	21	24	27	30
All patients	97	95	85	77	73	55	26	9	1	1	0	0
Responders with sCR	78	78	76	71	68	51	26	9	1	1	0	0

NE, not estimable; OS, overall survival; PFS, progression-free survival; sCR, stringent complete response.

Safety

- There were no new safety signals in CARTITUDE-1 with longer follow-up
- Cytokine release syndrome (CRS) occurred in 92 of 97 patients; of those, majority (94.6%) were grades 1/2
 - Median time to onset was 7 days (range, 1–12)
- CRS resolved in 91 (98.9%) patients within 14 days of onset
- No new incidence of neurotoxicity was observed with longer follow-up and no additional movement and neurocognitive treatment-emergent AEs (TEAEs) occurred
- New patient management strategies have been implemented in the CARTITUDE program to prevent and reduce the incidence of neurotoxicity (**Figure 5**)

Figure 5. Management Strategies for Movement and Neurocognitive AEs



*Defined as having high tumour burden when any of the following parameters were met: bone marrow plasma cell $\geq 80\%$, serum M-spike ≥ 5 g/dL, serum free light chain ≥ 5000 mg/L. *Included patients treated in earlier and later line settings across the CARTITUDE program. AE, adverse event; CAR-T, chimeric antigen receptor T cell; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event.

KEY FINDINGS STATEMENT

- A single infusion of cilta-cel yielded early, deep, and durable responses in heavily pretreated patients with MM, with no new safety signals with longer follow-up

CONCLUSIONS

- At a longer median follow-up of 18 months, a single dose of cilta-cel led to early, deep, and durable responses in heavily pretreated patients with MM
 - ORR: 98%; sCR: 80%; MRD 10^{-5} negativity: 92% in evaluable patients
 - 18-month PFS rate: 66%; OS rate: 81%
- Cilta-cel has a manageable safety profile consistent with its mechanism of action; no new safety signals were observed with longer follow-up
 - Successful new patient management strategies have been implemented in the CARTITUDE program to prevent and reduce the incidence of neurotoxicity
- Cilta-cel is being investigated in the ongoing phase 2 CARTITUDE-2 (NCT04133636) and phase 3 CARTITUDE-4 (NCT04181827) studies in earlier-line settings

REFERENCE

- Madduri D, et al. Blood 2020;136(Suppl 1):22-5.

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