

Administration of Ciltacabtagene Autoleucel (Cilta-cel), a B-Cell Maturation Antigen–Directed Chimeric Antigen Receptor T-Cell Therapy, in Relapsed/Refractory Multiple Myeloma

ICD-10 Coordination & Maintenance Committee Meeting March 9, 2021

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Presented on behalf of Janssen and Legend Biotech

Agenda



Cilta-cel Overview



Multiple Myeloma Paradigm Shift with A CART Therapy



Review of Manufacturing and Clinical Data



Conclusions: Substantial Clinical Evidence

CARTITUDE-1: Introduction

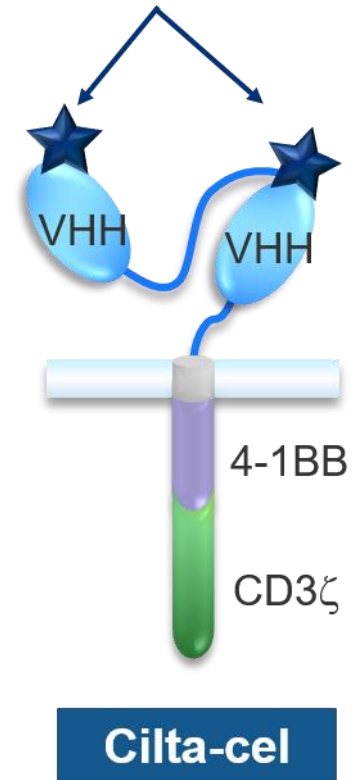
Ciltacabtagene autoleucel (cilta-cel; JNJ-68284528) is a chimeric antigen receptor T-cell therapy

2 BCMA-targeting single-domain antibodies designed to confer avidity

In the phase 1b portion of the CARTITUDE-1 study, cilta-cel yielded deep, durable responses with a manageable safety profile in patients with relapsed/refractory MM¹

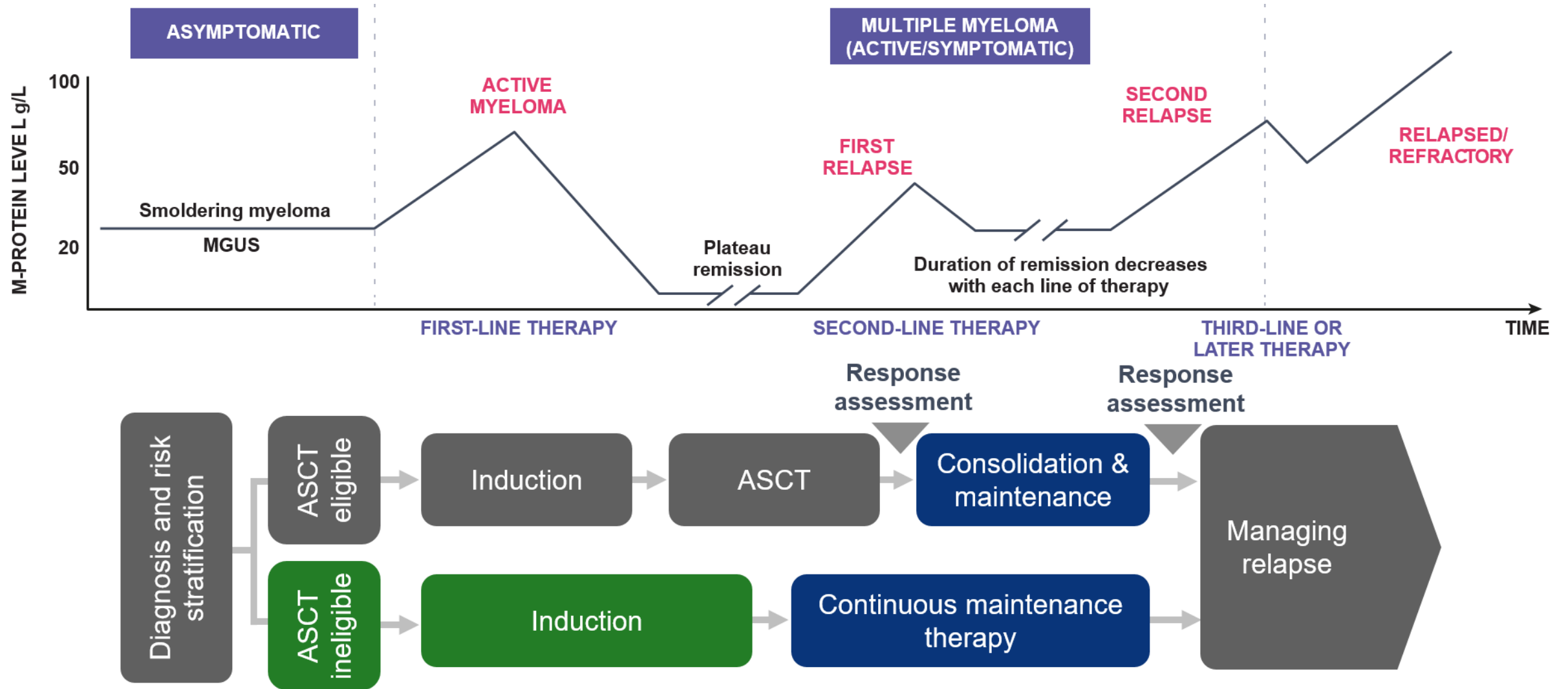
Here, we report initial results from the combined phase 1b/2 CARTITUDE-1 study of cilta-cel

Binding domains



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Treatment Overview



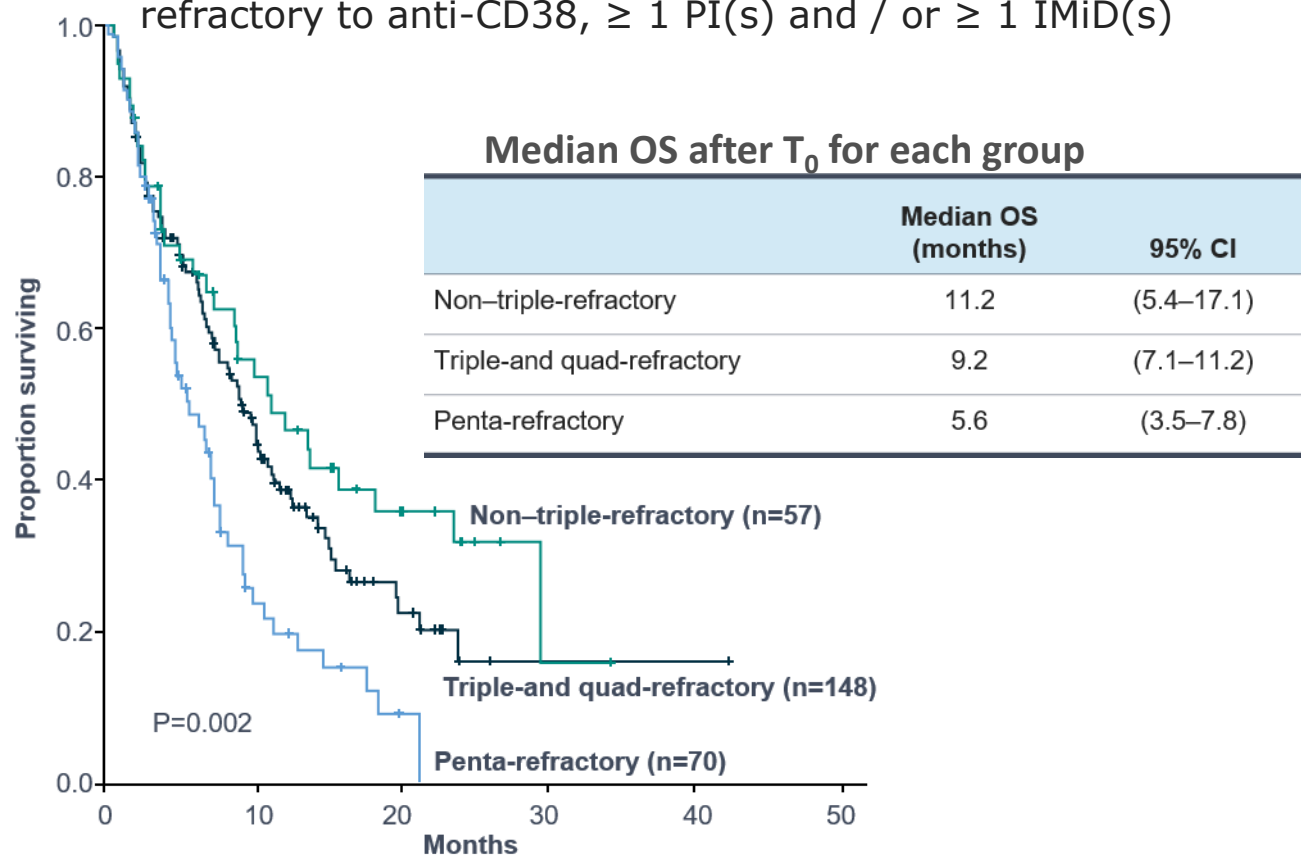
ASCT=autologous stem cell transplant; MGUS=monoclonal gammopathy of undetermined significance.

1. Kurtin SE. *J Adv Pract Oncol*. 2013;4(6 suppl 1):5–14.

2. Clinical Care Options Oncology. <https://www.clinicaloptions.com/oncology/programs/advances-in-multiple-myeloma/downloadable-slideset/advances-in-myeloma-slideset>. Accessed September 28, 2020.

Unmet Needs in the Treatment of Patients with Relapsed/Refractory Multiple Myeloma

Poor survival outcomes: median OS <12 months in patients refractory to anti-CD38, ≥ 1 PI(s) and / or ≥ 1 IMiD(s)



Current approved treatments

- Autologous SCT
- Chemotherapy
- Steroids
- PIs
- Immunomodulatory agents
- Monoclonal Antibodies (anti-CD38, SLAMF7)
- Other Agents

CD=cluster of differentiation; CI=confidence interval; IMiD=immunomodulatory drug; OS=overall survival; PFS=progression-free survival; RRMM=relapsed/refractory multiple myeloma; T₀=time point when patients met the criteria of disease progression.

Gandhi UK, et al. *Leukemia*. 2019; doi: <https://doi.org/10.1038/s41375-019-0435-7>.

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CARTITUDE-1: Phase 1b/2 Study of Ciltacabtagene Autoleucel, a B-Cell Maturation Antigen–Directed Chimeric Antigen Receptor T-Cell Therapy, in Relapsed/Refractory Multiple Myeloma

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CARTITUDE-1: Phase 1b/2 Study Design

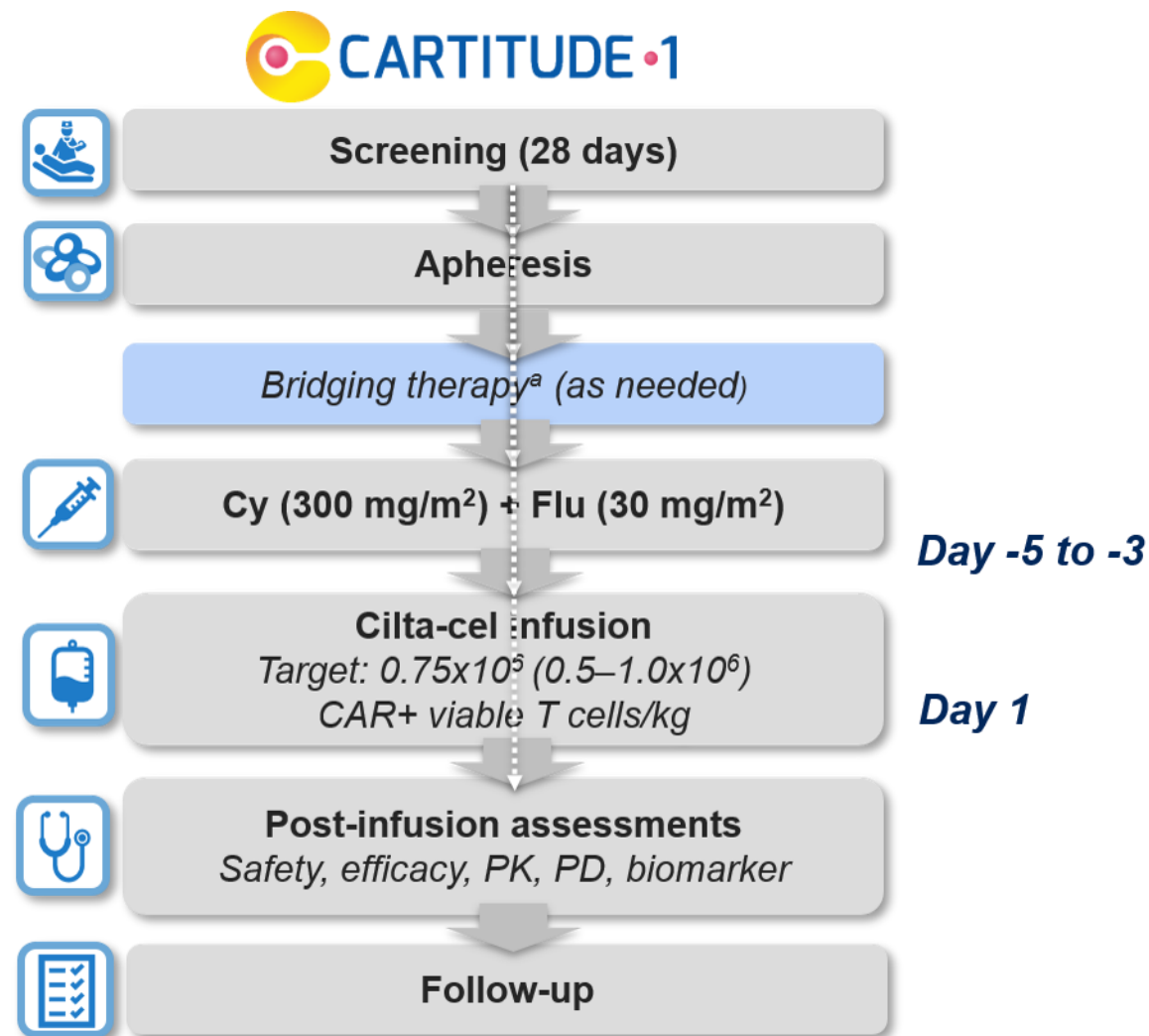
Primary objectives

Phase 1b: Characterize the safety of cilta-cel and confirm the recommended phase 2 dose

Phase 2: Evaluate the efficacy of cilta-cel by ORR

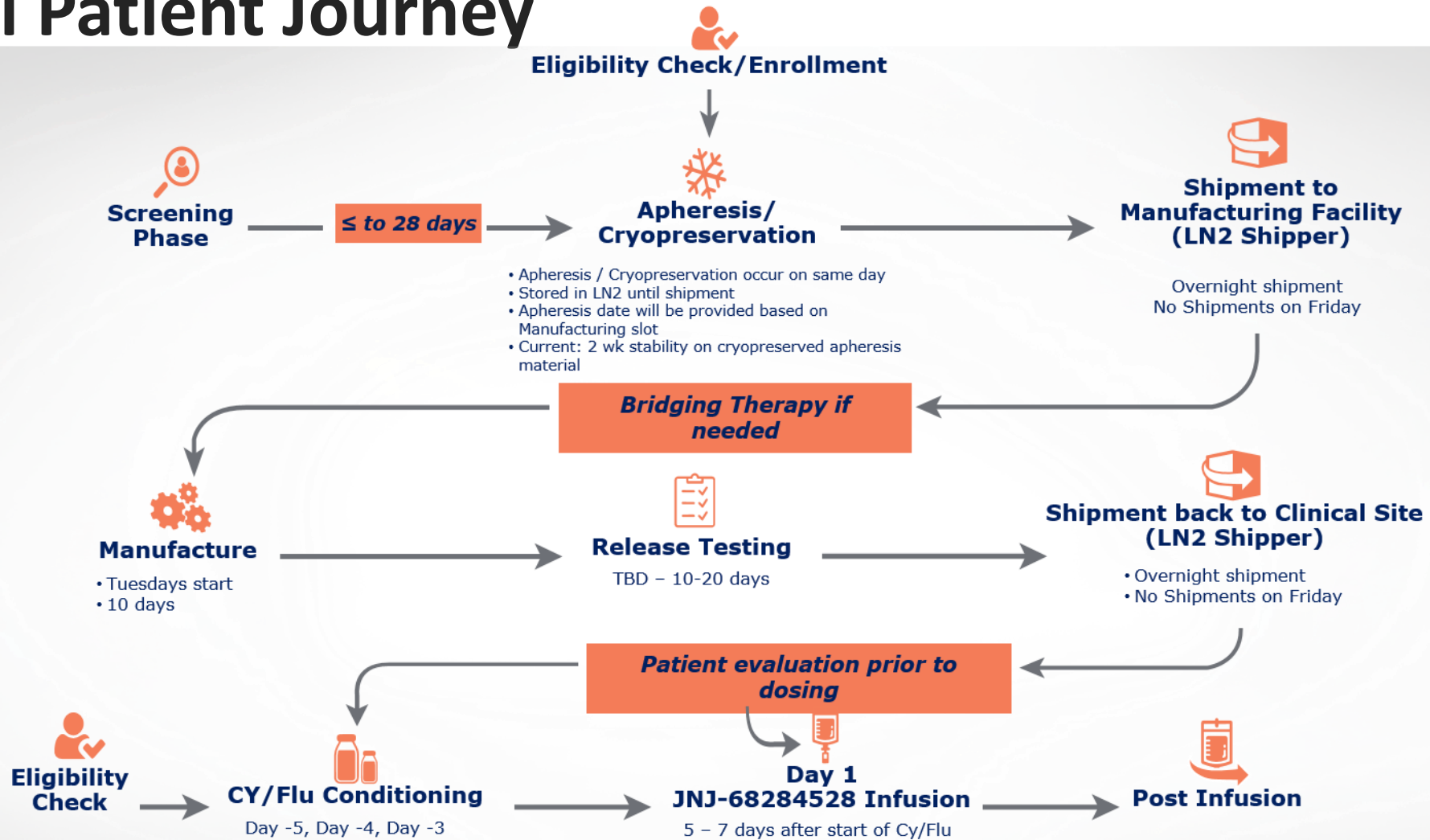
Key eligibility criteria

- Progressive MM per IMWG criteria
- ECOG PS ≤ 1
- Measurable disease
- ≥ 3 prior therapies or double refractory
- Prior PI, IMiD, anti-CD38 therapy
- Median administered dose: 0.71×10^6 (0.51 – 0.95×10^6) CAR+ viable T cells/kg

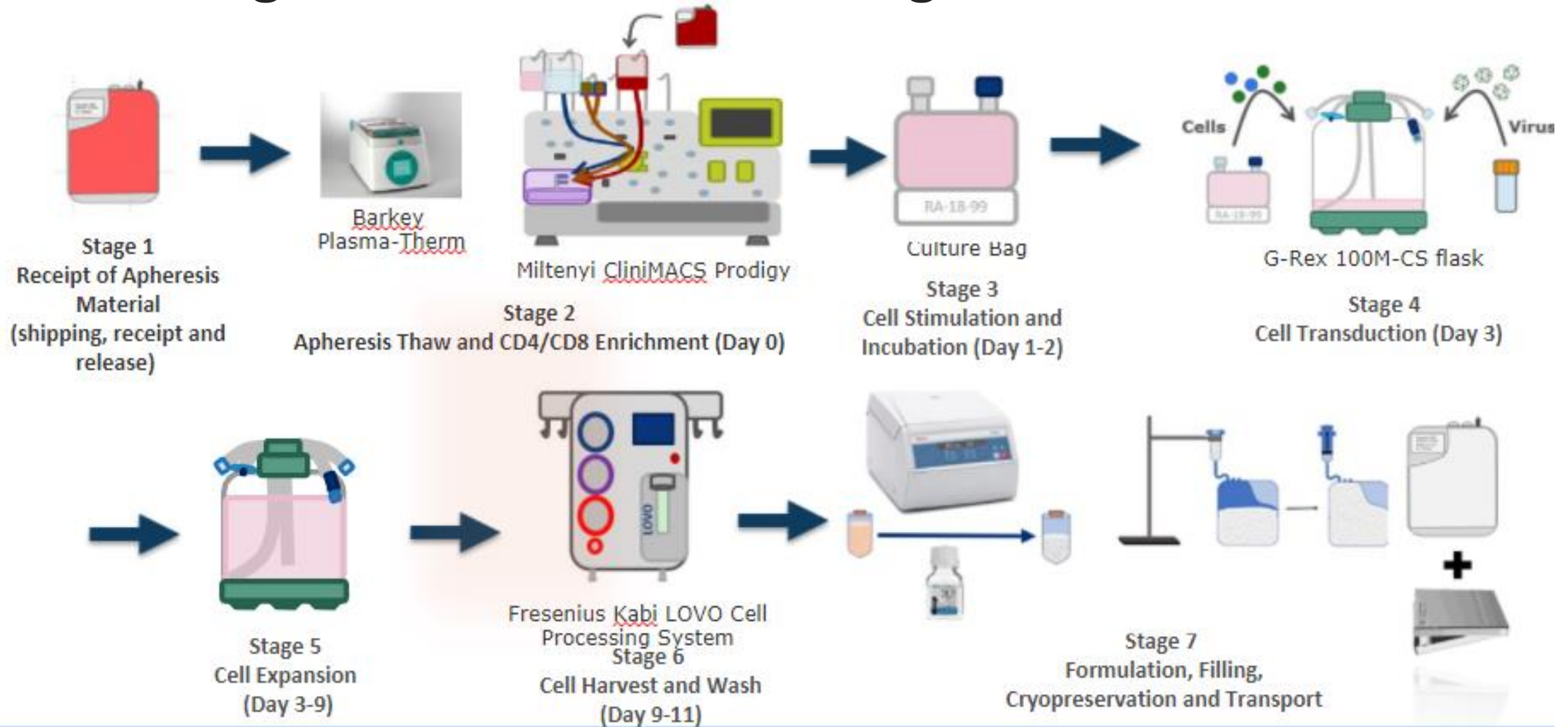


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Cilta-cel Patient Journey



Autologous CAR-T Manufacturing Process



Summary of Coding & Medical Documentation Points

Administration of cilta-cel:

- Administered via intravenous infusion -- central line or peripheral vein
- Similar to other approved CARTs (e.g., KYMRIAH and YESCARTA)

No current ICD-10-PCS codes are specific to cilta-cel

Information regarding cilta-cel, and its associated administration procedure, will be documented in the medical record and identifiable from multiple perspectives (e.g., physician orders, pharmacy notes, treatment summary)

CARTITUDE-1: Baseline Characteristics

Characteristic	N=97
Age, median (range) years	61.0 (43–78)
Male, n (%)	57 (58.8)
Extramedullary plasmacytomas ≥1, n (%)	13 (13.4) ^a
Bone-marrow plasma cells ≥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)
Tumor BCMA expression ≥50%, n (%)	57 (91.9) ^b

Characteristic	N=97
Prior lines of therapy, median (range)	6.0 (3–18)
Previous stem-cell transplantation, n (%)	
Autologous	87 (89.7)
Allogenic	8 (8.2)
Triple-class exposed, ^c n (%)	97 (100)
Penta-exposed, ^d n (%)	81 (83.5)
Triple-class refractory ^c	85 (87.6)
Penta-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)

BCMA, B-cell maturation antigen; IMiD, immunomodulatory drug; PI, proteasome inhibitor.

^aAdditional 6 patients had a soft-tissue component of a bone-based plasmacytoma (total plasmacytomas, 19.6%). ^bDenominator n=62, the number of evaluable samples; BCMA expression detected in all evaluable samples.

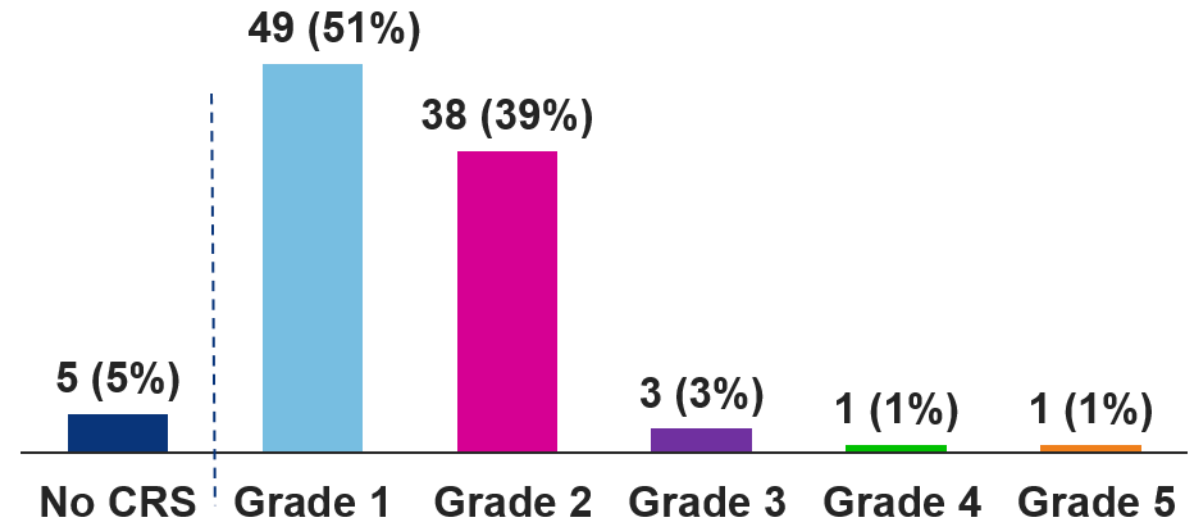
^cAt least 1 PI, at least 1 IMiD, and 1 anti-CD38 antibody. ^dAt least 2 PIs, at least 2 IMiDs, and 1 anti-CD38 antibody.

CARTITUDE-1: CRS

	N=97
Patients with a CRS event, ^a n (%)	92 (94.8)
Time to onset, median (range) days	7 (1–12)
Duration, median (range) days	4 (1–97) ^b
Supportive measures, n (%)	88 (90.7)
Tocilizumab	67 (69.1)
Corticosteroids	21 (21.6)
Anakinra	18 (18.6)
Vasopressor used	4 (4.1)
Intubation/mechanical ventilation	1 (1.0)
Other	
Cyclophosphamide	1 (1.0)
Etanercept	1 (1.0)

- Cilta-cel CAR+ T cells showed maximum peripheral expansion at a median of 13 days (range, 9–55)

Maximum CRS Grade (N=97)



Of 92 patients with CRS, majority (94.6%) were grades 1/2 CRS onset

– Day 4 or later: 89.1% (n=82)

– Day 6 or later: 73.9% (n=68)

CRS resolved in 91 (98.9%) patients within 14 days of onset

CARTITUDE-1: Neurotoxicity

Total CAR-T cell neurotoxicities

- Any grade: 20 (20.6%)
- Grade ≥ 3 : 10 (10.3%)

ICANS

- Any grade: 16 (16.5%)
- Grade ≥ 3 : 2 (2.1%)

Other neurotoxicities^a

- Any grade: 12 (12.4%)
- Grade ≥ 3 : 9 (9.3%)

	ICANS	Other neurotoxicities ^a
Time to onset, median (range) days	8 (3–12)	27 (11–108)
Time to recovery, median (range) days	4 (1–12)	75 (2–160)

Other neurotoxicities^a

- **Occurring after resolution of CRS and/or ICANS**
- Among 12 patients
 - 5 had AEs including movement and/or neurocognitive changes
 - 7 had AEs including nerve palsy, peripheral motor neuropathy

Outcomes for CAR-T cell neurotoxicities

ICANS resolved in all patients

Other neurotoxicities resolved in 6 patients, and did not resolve in 6 patients:

- 1 patient has ongoing neurotoxicity
- 1 patient died from complications of neurotoxicity
- 4 patients died due to other causes

No additional movement and neurocognitive AEs were seen in the CARTITUDE development program

AE, adverse event; CAR-T, chimeric antigen receptor T cell; CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome.

^aEvents not reported as ICANS [ie, onset after a period of recovery from CRS and/or ICANS]).

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CARTITUDE-1: Deaths

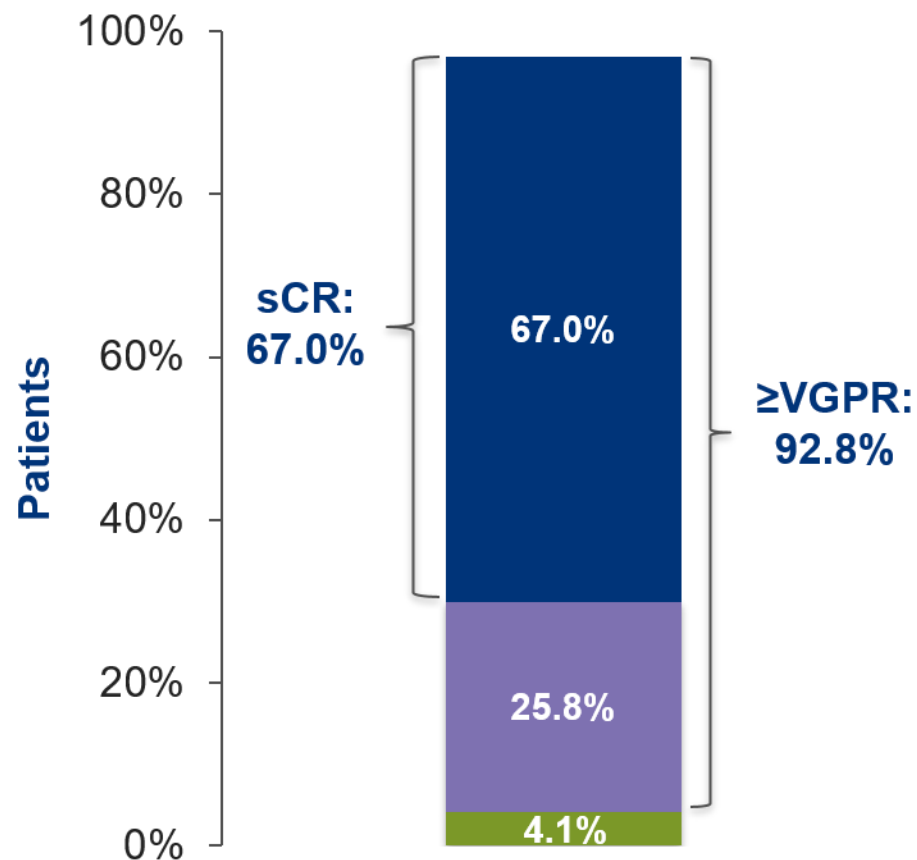
	N=97	Time of death post cilta-cel infusion, days
Total deaths during the study, n	14	45–694
Due to progressive disease	5	253–694
AEs unrelated to treatment (n=3)		
Pneumonia	1	109
Acute myelogenous leukemia ^a	2	418; 582
AEs related to treatment (n=6)		
Sepsis and/or septic shock	2	45; 162
CRS/HLH	1	99
Lung abscess	1	119
Respiratory failure	1	121
Neurotoxicity	1	247

AE, adverse event; CRS, cytokine release syndrome; HLH, hemophagocytic lymphohistiocytosis; MDS, myelodysplastic syndrome.

^aOne patient with acute myelogenous leukemia had MDS and a cytogenetic profile consistent with MDS (del20q [present prior to cilta-cel infusion], loss of 5q); the other had prostate cancer and squamous cell carcinoma of the scalp.

CARTITUDE-1: ORR and MRD Assessment

ORR^a: 96.9% (94/97)

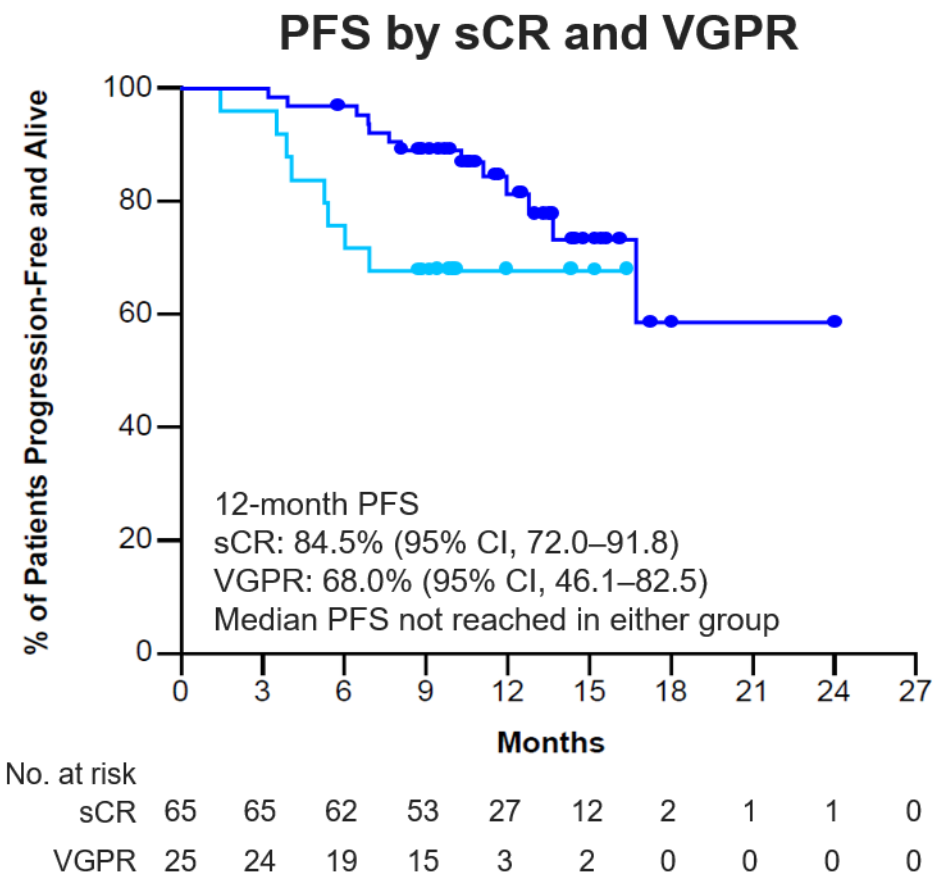
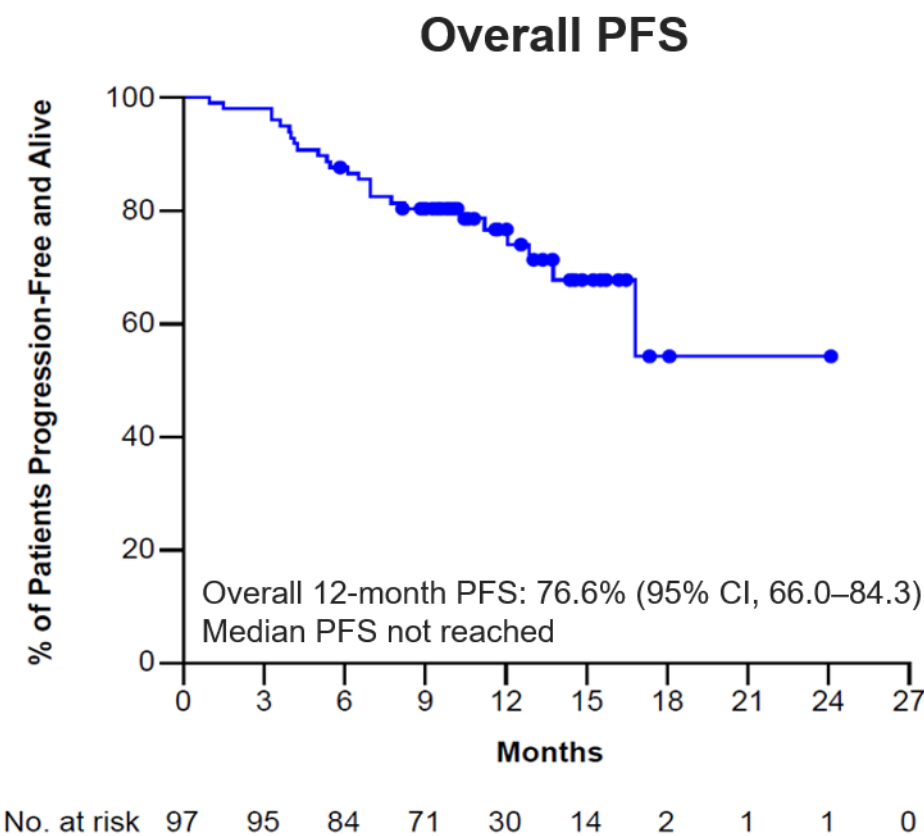


Best response^b = ■ sCR ■ VGPR ■ PR

	N	Frequency in evaluable patients n=57 ^c	Frequency in all treated n=97 ^d
Overall MRD-	53	93.0%	54.6%
MRD- and sCR	33	57.9%	34.0%
MRD- and ≥VGPR	49	86.0%	50.5%

- Median time to first response: 1 month (0.9–8.5)
- Responses ongoing in 70 (72.2%) patients
- Of evaluable patients, 93.0% achieved MRD 10⁻⁵ negativity
 - Median time to MRD 10⁻⁵ negativity: 1 month (0.8–7.7)
- Among patients with 6 months individual follow-up, most had cilta-cel CAR+ T cells below the level of quantification (2 cells/μL) in peripheral blood

CARTITUDE-1: PFS



At median duration of follow-up of 12.4 months (range, 1.5–24.9), median PFS has not been reached
12-month PFS rate: 76.6% (95% CI, 66.0–84.3)
12-month OS rate: 88.5% (95% CI, 80.2–93.5)

OS, overall survival; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

CARTITUDE-1: Conclusions

Cilta-cel has a manageable safety profile at the recommended phase 2 dose

- CRS was mostly grades 1/2; median time to onset of CRS was 7 days (range, 1–12)
- CAR-T-related neurotoxicities occurred in 20 patients (20.6%); 10.3% had grade ≥ 3

Low dose of cilta-cel yielded early, deep, and durable responses in heavily pretreated relapsed/refractory MM

- 96.9% ORR, with sCR 67.0%
- Median PFS not reached; 12-month PFS rate was 76.6%, OS rate was 88.5%

Cilta-cel is under further investigation in other populations of patients with MM in earlier-line settings

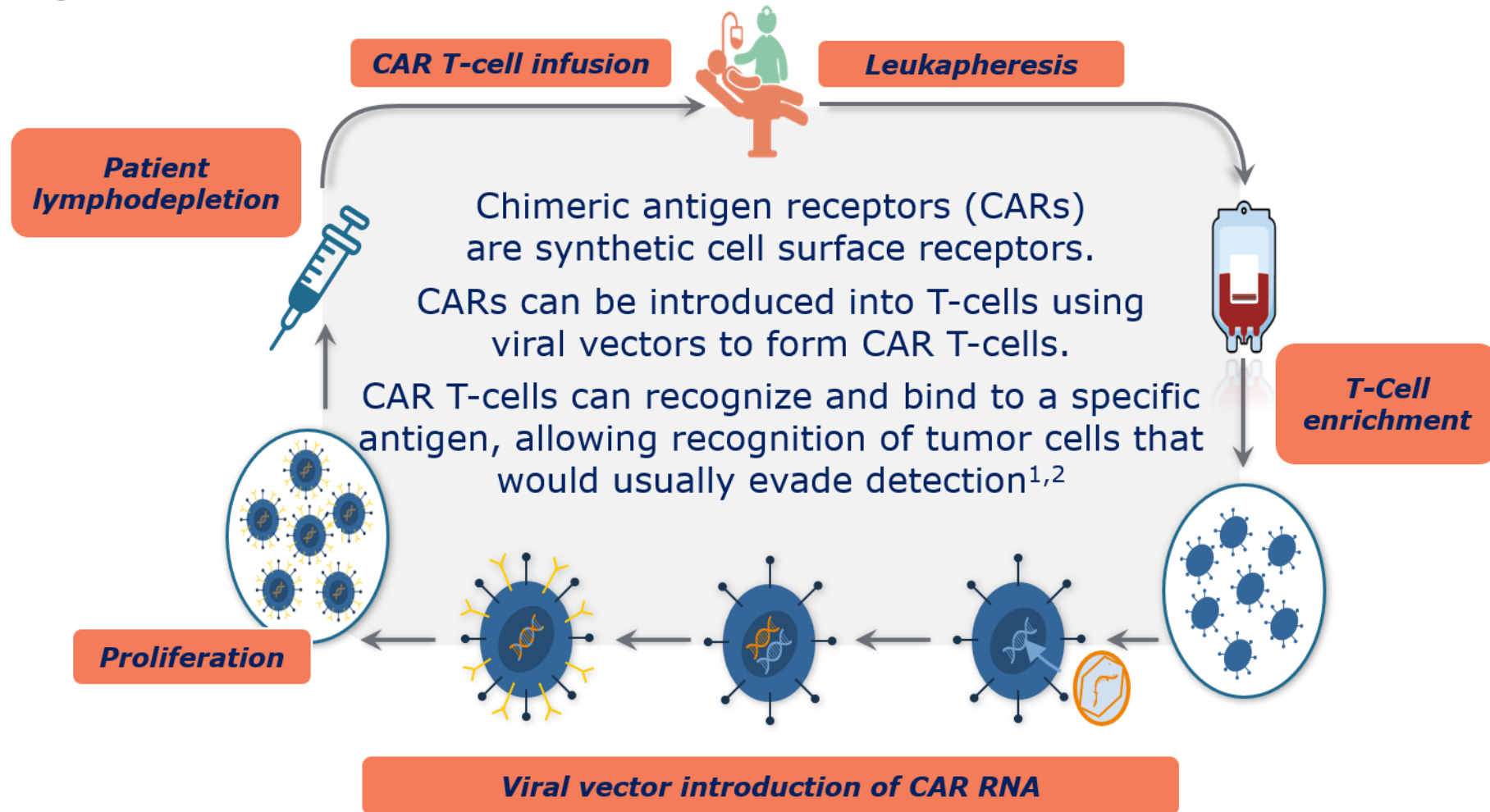
- Outpatient administration is being studied in CARTITUDE-2 (NCT04133636) and CARTITUDE-4 (NCT04181827)

AE, adverse event; CAR-T, chimeric antigen receptor T cell; CRS, cytokine release syndrome; MM, multiple myeloma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; sCR, stringent complete response.

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THANK YOU !

T-cells Can be Modified With CARs to Allow Them to Target Circulating Tumor



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