Real World CAR-T for Multiple Myeloma

Safety and Efficacy of Standard of Care Ciltacabtagene Autoleucel for Relapsed/Refractory Multiple Myeloma

Doris K. Hansen, MD
H. Lee Moffitt Cancer Center & Research Institute
Department of Blood & Marrow Transplant & Cellular Immunotherapy

Cell Coast Conference
Tampa, Florida, USA
October 26, 2024

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Disclosures

Research funding

- Bristol Myers Squibb/Celgene, Janssen, Adaptive Biotechnologies, and Karyopharm.
- Additional funding from Pentecost Myeloma Research Center, Myers Foundation, Schulze and M-CARES awards (pilot grants) via Moffitt Cancer Center.
- NCI/R01CA281756-01A1

Consultant

- Bristol Myers Squibb/Celgene, Janssen, Legend Biotech, Karyopharm, Kite Pharma, and Pfizer.

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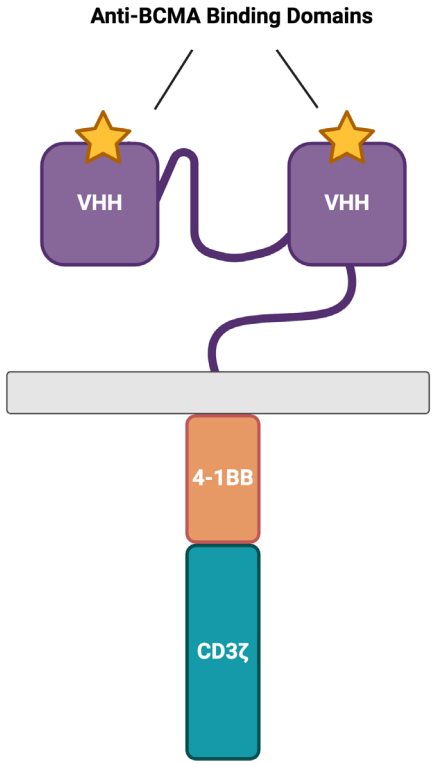
Background

- Cilta-cel is an autologous BCMA targeted CAR-T therapy
- Approved in the US in 2022 and now available in many other countries
- Initial approval for for patients with RRMM with 4 or more prior lines of therapy including PI, IMiD and anti-CD38 antibody
- In the pivotal CARTITUDE-1 clinical trial, 97 patients received cilta-cel



	CARTITUDE-1, N=97
ORR	98%
CR rate	83%
PFS	34.9 months

1. Berdeja et al. Lancet 398:314-324, 2021; 2. Martin et al. J Clin Oncol 41:1265-1274, 2023. 3, Lin et al ASCO 2023

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Study Design

- **Objective:** Describe safety and efficacy of standard-of-care (SOC) cilta-cel in patients with RRMM
- **Retrospective analysis:** Patients at 16 U.S centers
- **Population description:** RRMM patients who underwent apheresis with intent to manufacture SOC cilta-cel until Dec 31st 2022

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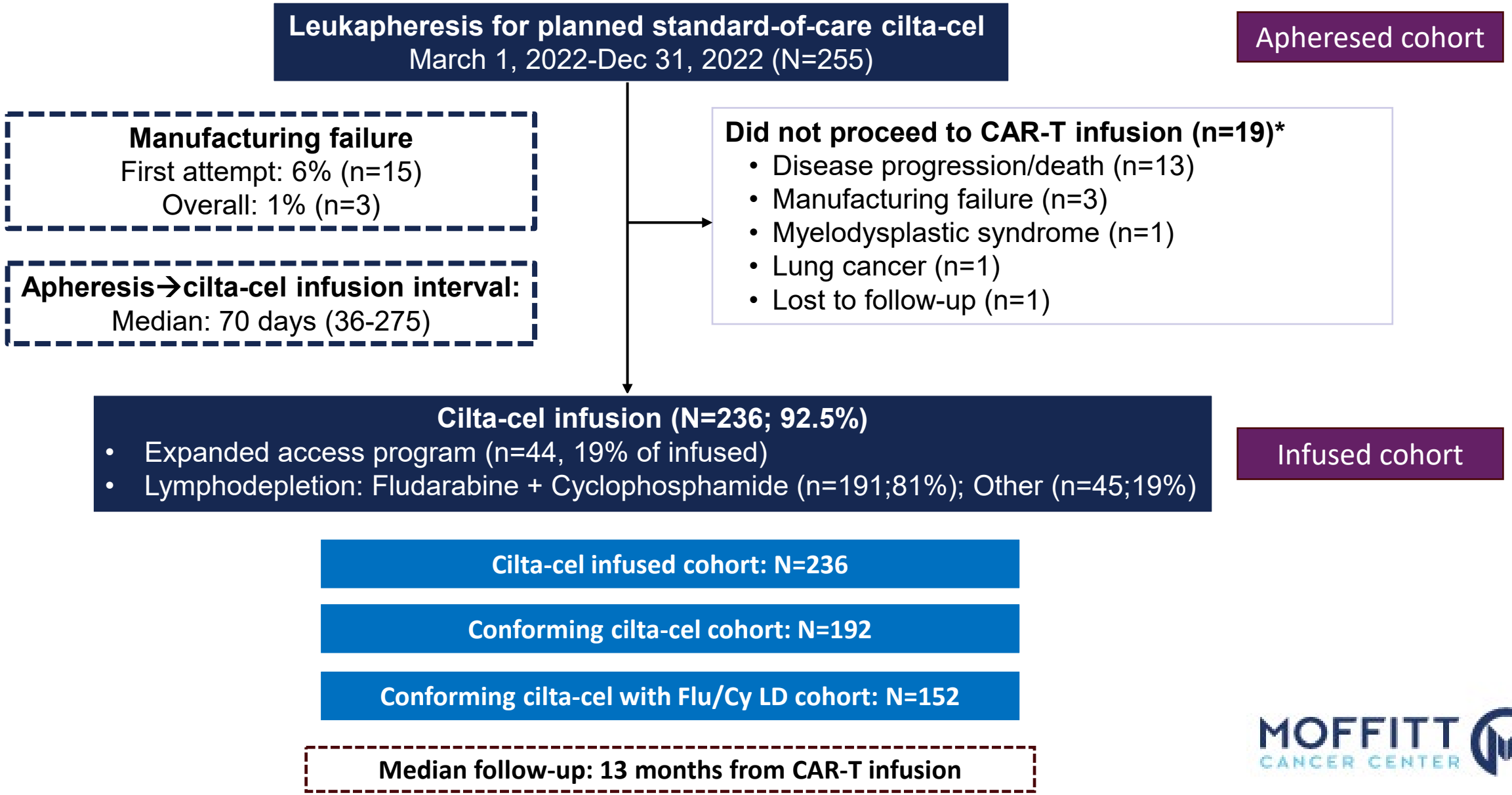
Cilta-Cel Consort Diagram



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Real World Study Population Characteristics in relation to Pivotal CARTITUDE-1 trial

Real-world patients who would have been ineligible for participation in the pivotal CARTITUDE-1 trial

56% (N=144) of apheresed patients
54%(N=128) of infused patients

CARTITUDE-1 trial Exclusion Criteria at leukapheresis	Apheresed patients N=144 (56%)	Infused patients N=128 (54%)
Organ dysfunction (renal, cardiac, hepatic)	31 (13%)	27 (12%)
Creatinine clearance < 40 ml/min	22 (9%)	18 (8%)
Prior anti-BCMA therapy	38 (15%)	33 (14%)
Cytopenias	45 (18%)	37 (16%)
ECOG PS ≥ 2	28 (11%)	25 (11%)
Active or prior plasma cell leukemia, amyloidosis or POEMS	28 (11%)	24 (10%)
H/o CNS myeloma/other CNS pathology	12 (5%)	12 (5%)

Amongst all patients missing data for organ dysfunction in 9 patients, creatinine clearance in 1, cytopenias in 1 and performance status in 1.
Amongst infused patients: missing data for organ dysfunction in 8 patients, creatinine clearance in 1, cytopenias in 1 and performance status in 1.

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Baseline Characteristics of Infused Patients

	RWE Cilta-cel (N=236)	CARTITUDE-1 (N=97)[1]
Age, median (range)	64 y (30-84)	61 y (56-68)
Age ≥ 70 years	62 (26%)	-
Race: Black	26 (11%)	17 (18%)
Ethnicity: Hispanic	19 (8%)	6 (6%)
ECOG PS, 0-1	183 (89%)	93 (96%)
High-risk cytogenetics*	81 (39%)	23 (24%)
R-ISS stage III	30 (19%)	ISS-3:14 (14%)
Extramedullary Disease**	60 (26%)	13 (13%)
BM Plasma cells ≥ 50%	35 (18%)	≥ 60%= 21 (22%)
H/o plasma Cell Leukemia	13 (6%)	0
H/o AL amyloidosis	8 (3%)	0

*High-risk cytogenetics: Del 17p, t(14;16), t(4;14)
**EMD included patients with plasmacytomas non-contiguous from bone lesions

	RWE Cilta-cel (N=236)	CARTITUDE-1 (N=97)[1]
Prior Lines of Therapy	6 (2-18)	6 (4-8)
Prior Auto SCT	200 (85%)	87 (90%)
Triple Class Refractory	163 (69%)	85 (88%)
Penta Drug refractory	70 (30%)	41 (42%)
Prior BCMA Therapy	33 (14%)	0%
Bridging Therapy	184 (78%)	73 (75%)
PR (≥ 50%) to Bridging	44 (27%)	15 (21%)
Elevated baseline ferritin > 400 ng/mL	82 (35%)	-
Flu/Cy Lymphodepletion	191 (81%)***	97 (100%)

*** Alternate lymphodepletion, bendamustine: 31(13%), cladribine + cyclophosphamide: 6 (3%); cyclophosphamide alone: 7 (3%), NA:1

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1. Berdeja et al. Lancet 398:314-324, 2021.

Safety of SOC Cilta-cel

	Real-world N=236	CARTITUDE-1 [1-2] N=97
CRS - Any grade	177 (75%)	95%
Grade ≥ 3	12 (5%)	4%
Median time to onset of CRS	7 days (0-14)	
ICANS – Any grade	32 (14%)	17%
Grade ≥ 3	9 (4%)	2%
Delayed neurotoxicity	24 (10%)	12%
Parkinsonism	5 (2%)	6%
Cranial nerve palsy	11 (5%)	-
Others	8	
IEC-HS/HLH	5 (2%)	~1%
Severe infections	49 (21%)	20%

Other delayed NT: Diplopia in 4, posterior reversible encephalopathy syndrome (PRES) in 2, dysautonomia in 1 patient, and polyneuropathy in 1 patient

Multivariable Analysis:

- **Grade ≥ 2 CRS**: poor performance status and high baseline ferritin increased risk
- **ICANS**: poor performance status and penta-refractory status increased risk

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1. Berdeja et al. Lancet 398:314-324, 2021; 2. Martin et al. J Clin Oncol 41:1265-1274, 2023.

Safety of SOC Cilta-cel

	Real-world N=236
Non-relapse mortality (NRM)	**23 (10%)**
• Infections	12
• CRS	3
• CRS and infection	1
• Delayed neurotoxicity	3
• IEC-HS	2
• ICANS	1
• SPM	1
SPMs	**20 (8.5%)**
Excl. non-melanoma skin cancer	13 (5.5%)
Myeloid neoplasm/acute leukemia	3 (1.3%)
T cell lymphoma	1

NRM in CARTITUDE-1: 6%
In CARTITUDE-1: 16 deaths due to reasons other than progression. Only 6 of 16 deaths non-myeloma related deaths attributed to cilta-cel per investigator assessment (6%)

SPMs in CARTIUDE-1:
- At 1-year median follow-up, SPM rate was 7% including 5 cases of MDS and 2 of acute leukemia[1]
- At 2-year median follow-up, SPM rate was 16.5% including 8% myeloid neoplasms and acute leukemia[2]

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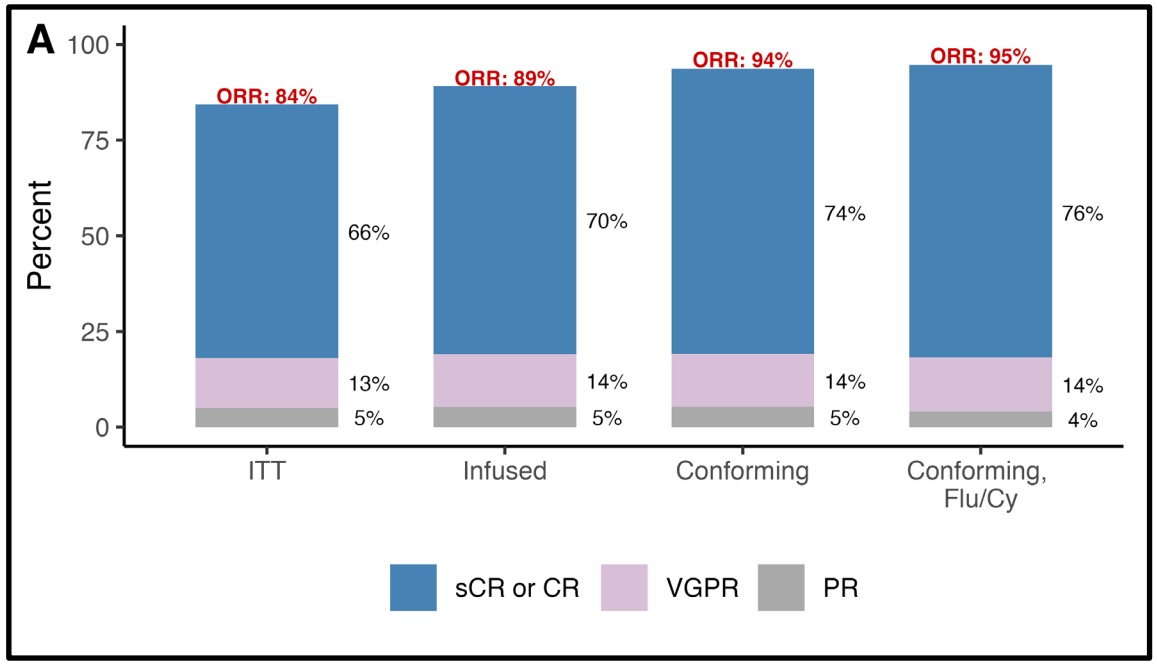
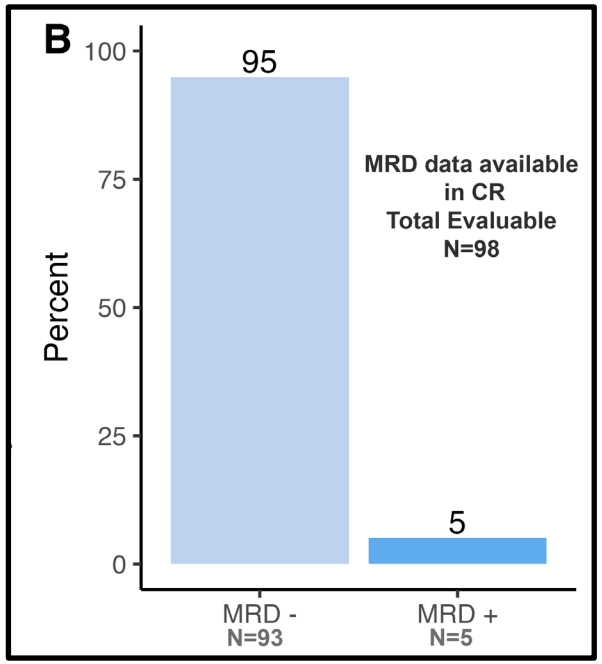
1. Berdeja et al. Lancet 398:314-324, 2021; 2. Martin et al. J Clin Oncol 41:1265-1274, 2023.

SOC Cilta-cel: Response Rates

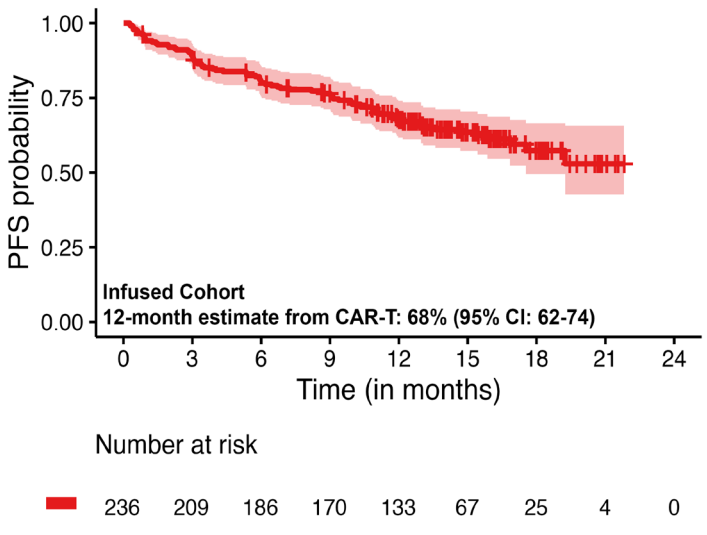


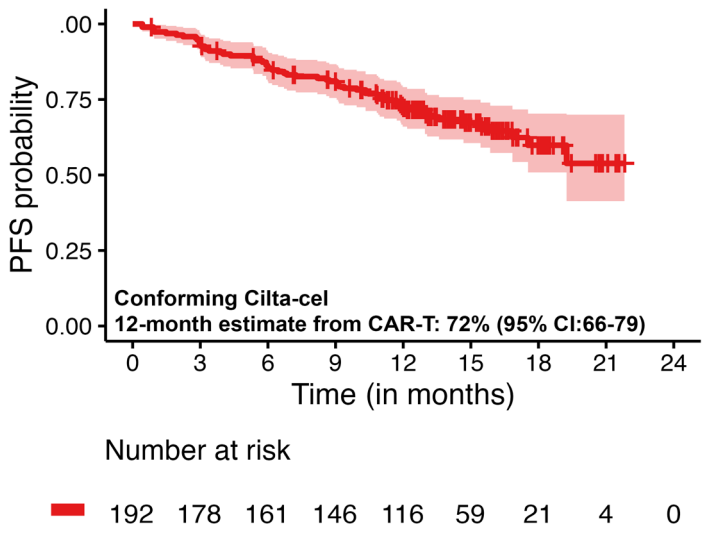


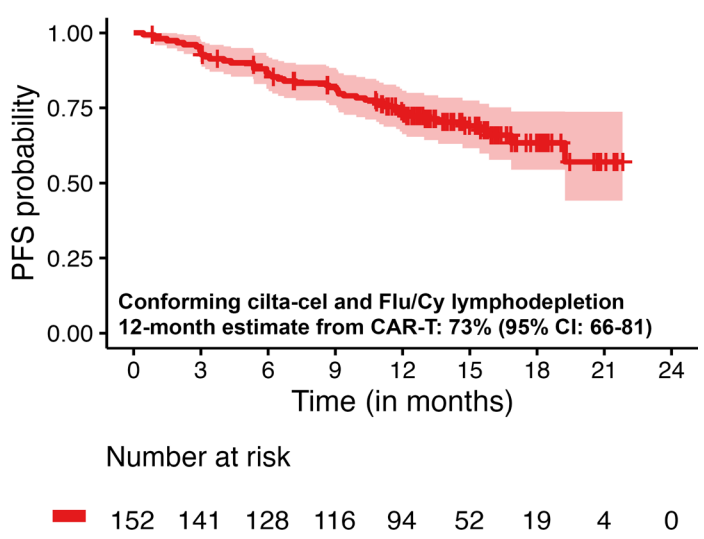
	Real-world N=236	Conforming N=192	Conforming+ Flu/Cy, N=152	CARTITUDE-1[1-3] N=97
ORR	89%	94%	95%	98%
CR rate	70%	74%	76%	83%

1. Berdeja et al. Lancet 398:314-324, 2021; 2. Martin et al. J Clin Oncol 41:1265-1274, 2023. 3. Lin et al ASCO 2023

Progression Free Survival







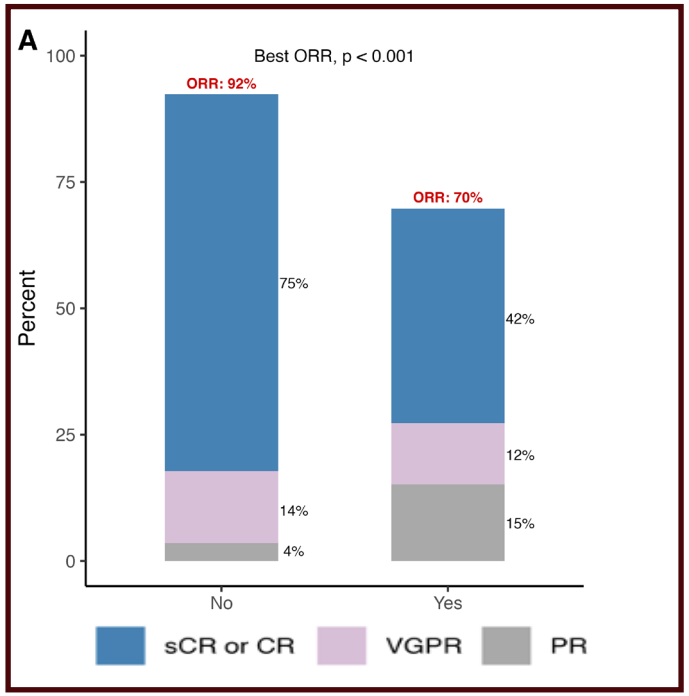
Median follow-up: 13 months from CAR-T infusion

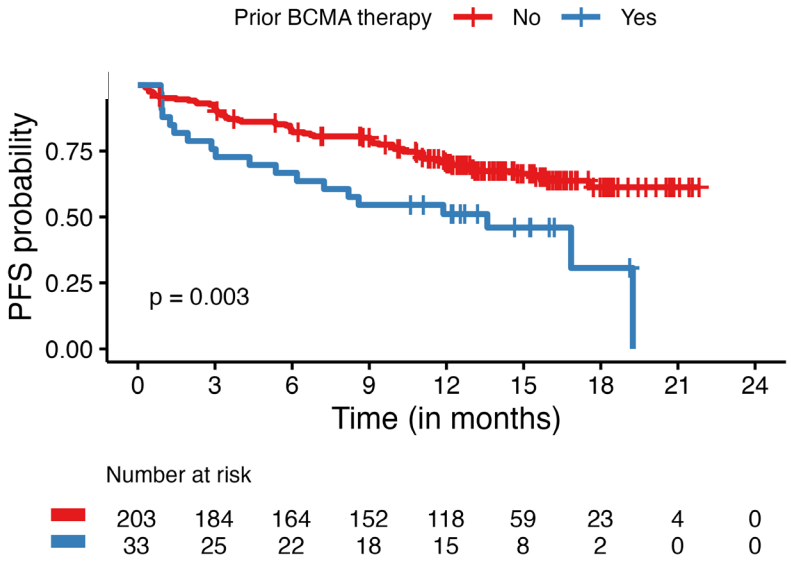
	Infused cohort N=236	Conforming cilta-cel N=192	Conforming + Flu/Cy LD N=152	CARTITUDE-1 [1-3] N=97
PFS: 12-month estimate (95% CI)	68% (62-74)	72% (66-99)	73% (66-81)	12m : 77%[1] Median: 34.9 m

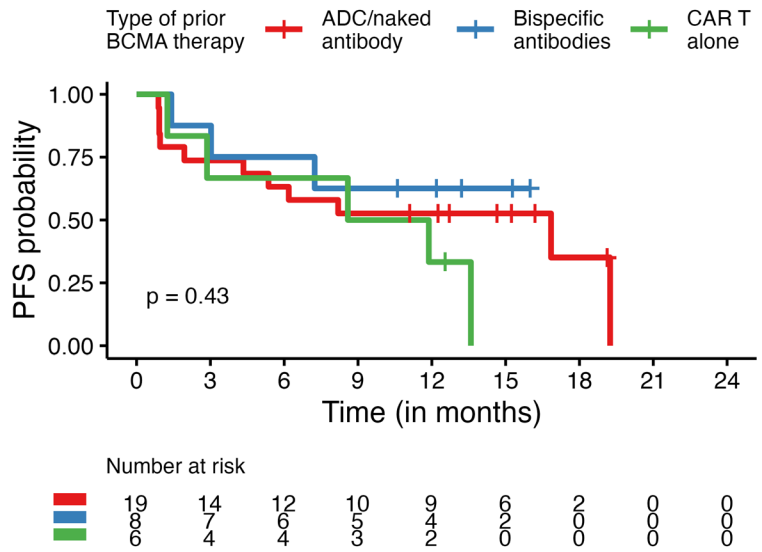
1.. Berdeja et al. Lancet 398:314-324, 2021; 2. Martin et al. J Clin Oncol 41:1265-1274, 2023. 3. Lin et al ASCO 2023

Cilta-cel after Prior BCMA-directed Therapy

Type of prior BCMA Therapy	N=33/236 (14%)
Prior ADC/naked antibody (n=1)	16
Prior ADC and CAR-T	2
Prior ADC + BCMA bispecific Ab	1
Prior BCMA bispecific Ab	8
Prior CAR-T cell therapy	6







Prior BCMA Directed therapy

- **ORR: 70%**
- **CR rate: 42%**
- **Median PFS: 13.6 months**

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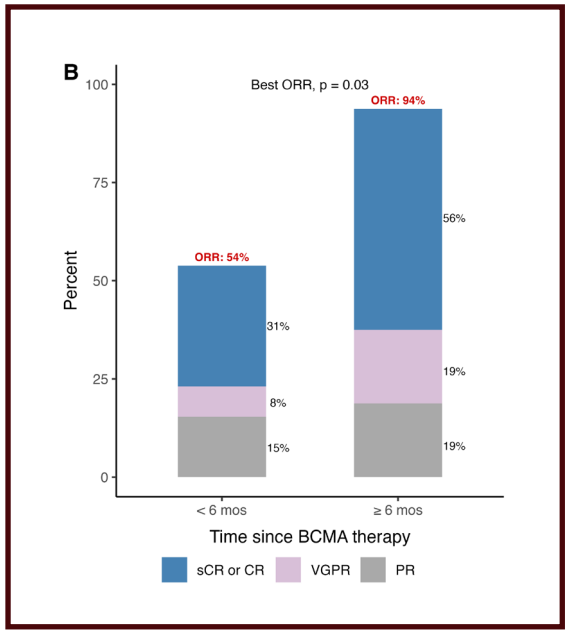
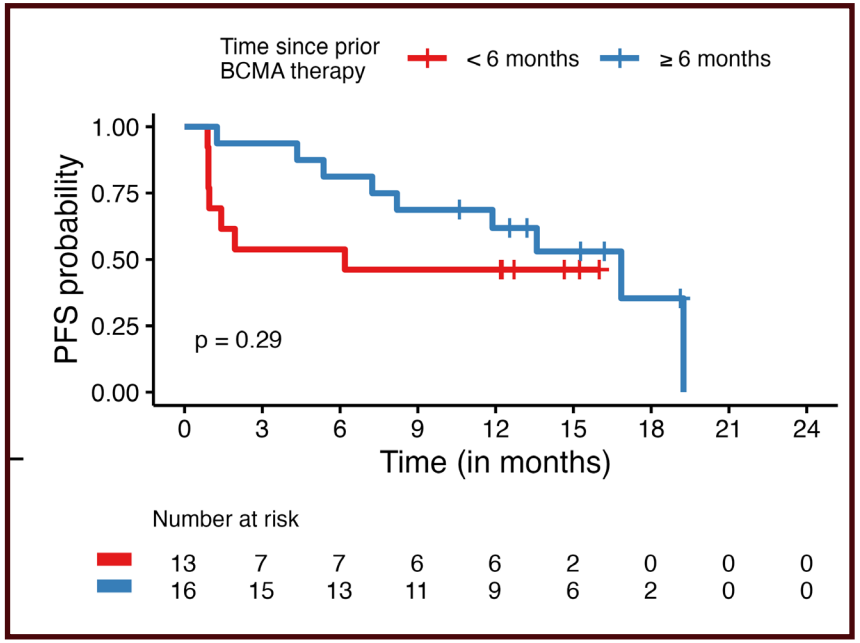
Cilta-cel after Prior BCMA Therapy: Timing Matters!

Time from last BCMA Therapy Exposure	N=29/33
Median time	7.1 months
≥ 6 months	16 (55%)
< 6 months	13 (45%)
Unknown	4





Patients with last BCMA targeted therapy < 6 months prior to cilta-cel had lower response rates and numerically lower PFS

Efficacy Measure	Last BCMA exposure ≥6 vs < 6 months
Overall response Rate	54% vs 94%, p=0.03
Complete Response Rate	31% vs. 56% p=0.2
Median PFS	6.2 vs 16.8 months, p=0.29

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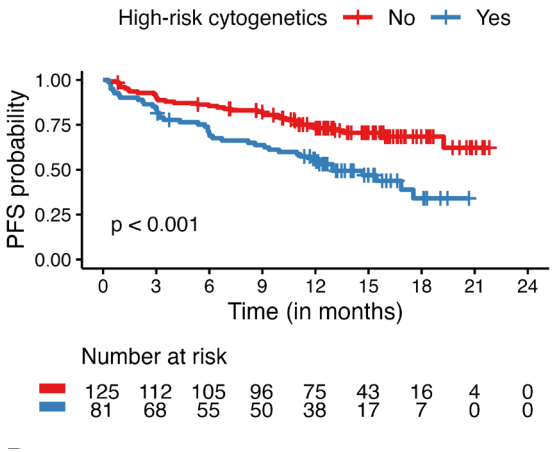
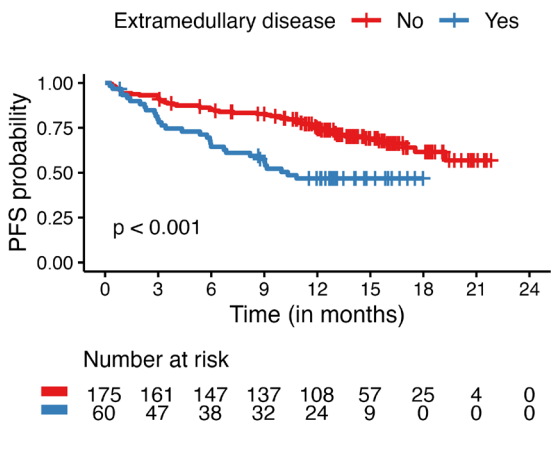
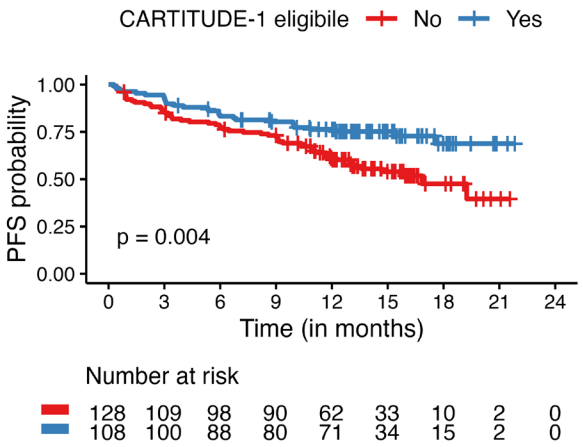
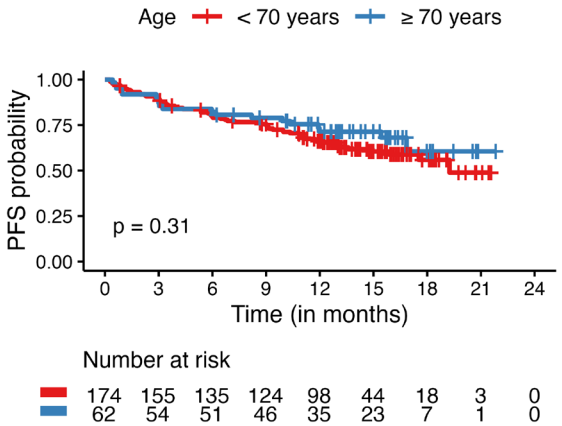
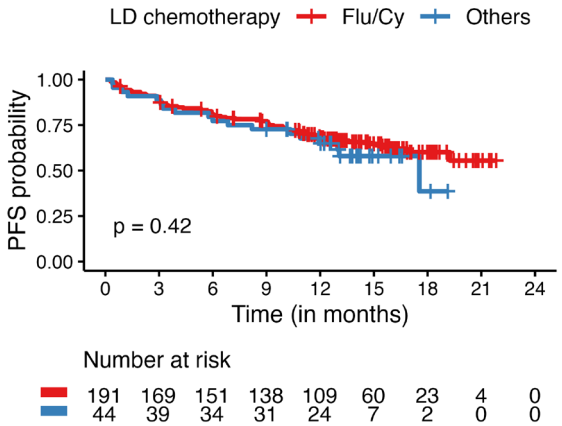
PFS: Sub-Groups of Interest











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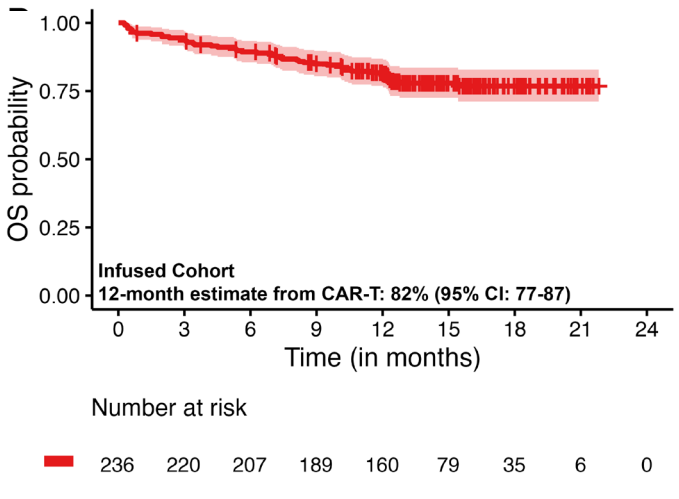
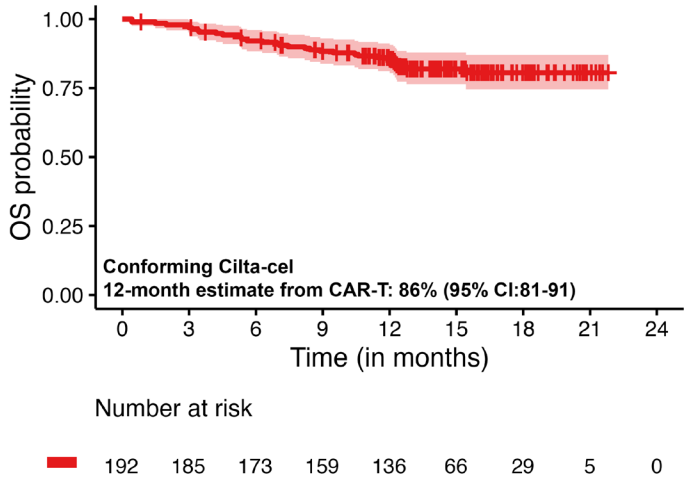
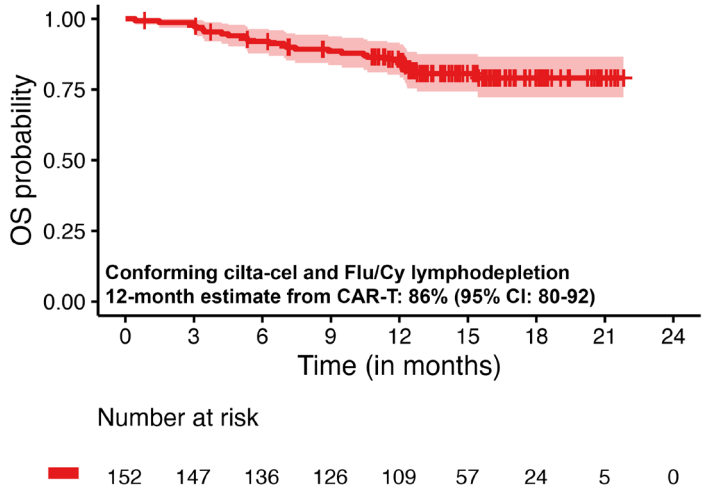
Overall Survival







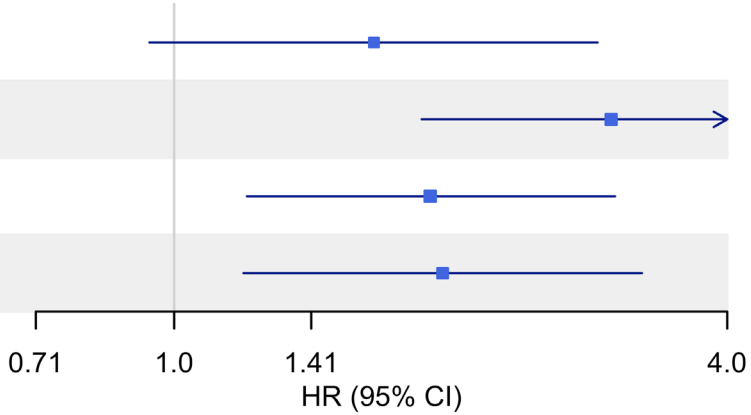
	Infused cohort N=236	Conforming cilta-cel N=192	Conforming+Flu/Cy LD N=152	CARTITUDE-1 [1-3] N=97
OS 12-month estimate (95% CI)	82% (77-87)	86% (81-91)	86% (80-92)	89%[1]

1. Berdeja et al. Lancet 398:314-324, 2021; 2. Martin et al. J Clin Oncol 41:1265-1274, 2023. 3. Lin et al ASCO 2023

Multivariable Analysis: PFS and OS

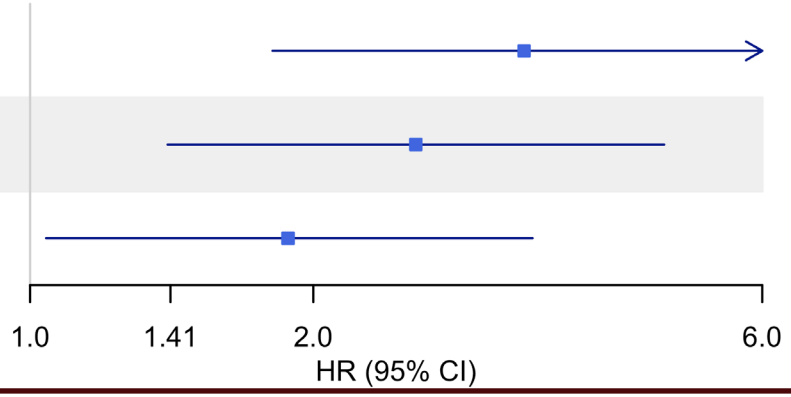
PFS

Variable	HR (95% CI)	P-value
Prior BCMA-TT (Yes vs. No)	1.65 (0.94, 2.89)	0.08
Ferritin (≥ 400 vs. < 400 ng/mL)	2.99 (1.86, 4.80)	<0.001
High-risk cytogenetics (Yes vs. No)	1.90 (1.20, 3.02)	0.006
Extramedullary disease (Yes vs. No)	1.96 (1.19, 3.23)	0.009



OS

Variable	HR (95% CI)	P-value
Ferritin (≥ 400 vs. < 400 ng/mL)	3.35 (1.81, 6.19)	<0.001
High-risk cytogenetics (Yes vs. No)	2.57 (1.40, 4.72)	0.005
Extramedullary disease (Yes vs. No)	1.88 (1.04, 3.42)	0.04



Cox Proportional Hazards model using a stepwise variable selection approach.

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Conclusions

- Cilta-cel administration is feasible in a real-world population of patients with RRMM.
- Cilta-cel resulted in high response rates (89-95%), that were deep and durable in heavily pre-treated patients (1-year PFS: 68-73%), despite over half of the patients being ineligible for the pivotal trial.
- Toxicity profile was consistent with clinical trial data. Future monitoring of SPMs and measures to manage delayed neurotoxicities and decrease NRM are needed.

Delayed NT: 10%
Parkinsonism: 2%

SPMs with 13 m follow-up: 8.5%
Excl. non-melanoma skin cancer: 5.5%

Non-relapse mortality: 10%

Prior BCMA Directed Therapy → Lower response rate and PFS.

→

Least favorable outcomes with BCMA exposure < 6 months prior to cilta-cel

High-risk cytogenetics, EMD and elevated ferritin → independent adverse prognostic factors for PFS

Thank you: U.S. Multiple Myeloma Immunotherapy Consortium Sites