CARVYKTI® (Cilta-cel) for the Treatment of Relapsed and Lenalidomide-Refractory Multiple Myeloma

March 15, 2024

Oncologic Drugs Advisory Committee

Johnson & Johnson Innovative Medicine

Introduction

Sen Zhuang, MD, PhD

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Johnson & Johnson

CARVYKTI (Cilta-cel) is BCMA-Directed CAR-T Therapy

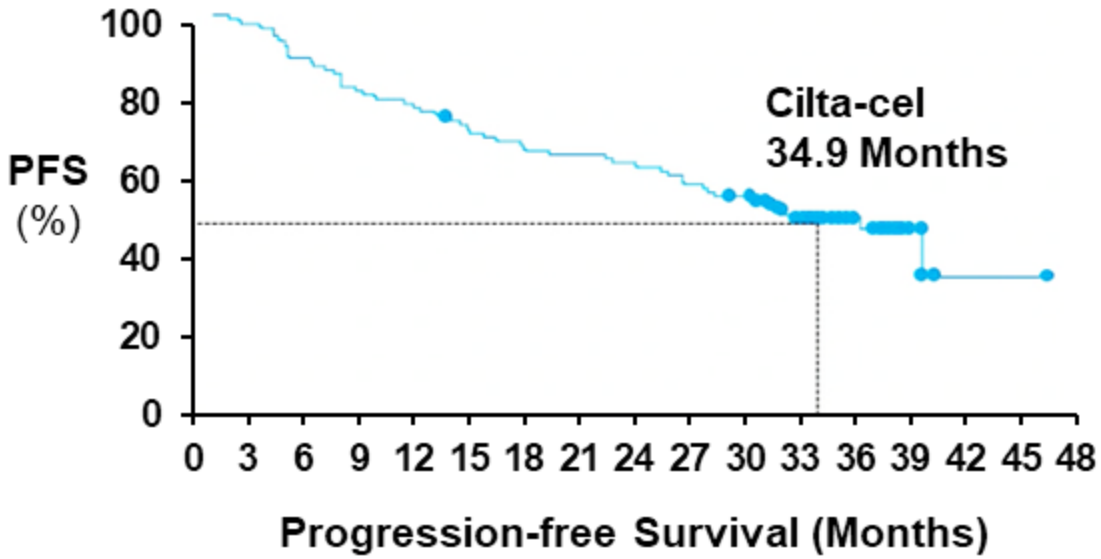
- Genetically engineered from patients' T cells to target Multiple Myeloma (MM)
- US approval in February 2022 for relapsed refractory MM (RRMM) after ≥ 4 prior lines of therapy including a PI, an IMID, and an anti-CD38 antibody

CARVYKTI (Cilta-cel) has Emerged as Transformative One-Time Infusion Therapy for Advanced RRMM

CARTITUDE-1

	Cilta-cel (N = 97)
ORR, n **(%)**	**97.9%**
sCR	82.5%
VGPR	12.4%
PR	3.1%
DOR, median (95% CI)	**33.9** (25.5, NE)

Martin, 2023



Jagannath, 2023

CARTITUDE-4 Supports Cilta-cel's Positive Benefit-Risk for Lenolidomide-Refractory MM

- Randomized controlled Phase 3 study of cilta-cel in patients with 1 – 3 lines of prior treatment and refractory to lenalidomide
  - Poor outcome in lenalidomide-refractory RRMM: median PFS ~ 12 months

Efficacy

- Clinically meaningful, highly statistically significant PFS vs SoC
- Complete, deep, durable responses translate into improved OS that strengthens as data mature
- Consistent benefit across subgroups

Safety

- Safety consistent with known safety of approved cilta-cel and MoA of CAR-T therapy
- Early imbalance in PFS and OS driven by patients who did not receive cilta-cel, and not due to cilta-cel toxicity

Proposed Indication

CARVYKTI is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma, who have received at least 1 prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent, and are refractory to lenalidomide.

Agenda

Unmet Need

Irene Ghobrial, MD
Professor of Medicine
Dana Farber Cancer Institute
Harvard Medical School

Efficacy and Safety

Jordan Schecter, MD
Vice President
Research & Development
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Clinical Perspective

Sundar Jagannath, MD
Director of Center of Excellence for Multiple Myeloma Tisch Cancer Institute
Professor of Medicine at Icahn School of Medicine Mount Sinai

Additional Experts

Janet Wittes, PhD	Consultant Statistician
Yi Lin, MD, PhD	Professor of Medicine, Mayo Clinic
Nikoletta Lendvai, MD, PhD	Clinical Leader, Johnson & Johnson
Loreta Marquez, MD	Safety Head Cellular Therapy, Johnson & Johnson
Tzu-Min Yeh, MS	Global Statistical Leader, Johnson & Johnson
Brent Williams, PhD	Global CARVYKTI Platform Head, Johnson & Johnson
Vicki Plaks, LLB, PhD	Senior Scientific Director, Head of Cell Therapy, Oncology Translational Research, Johnson & Johnson
Katie Gries, PharmD, PhD	Senior Director, Patient Reported Outcomes, Johnson & Johnson

Unmet Need

Irene Ghobrial, MD

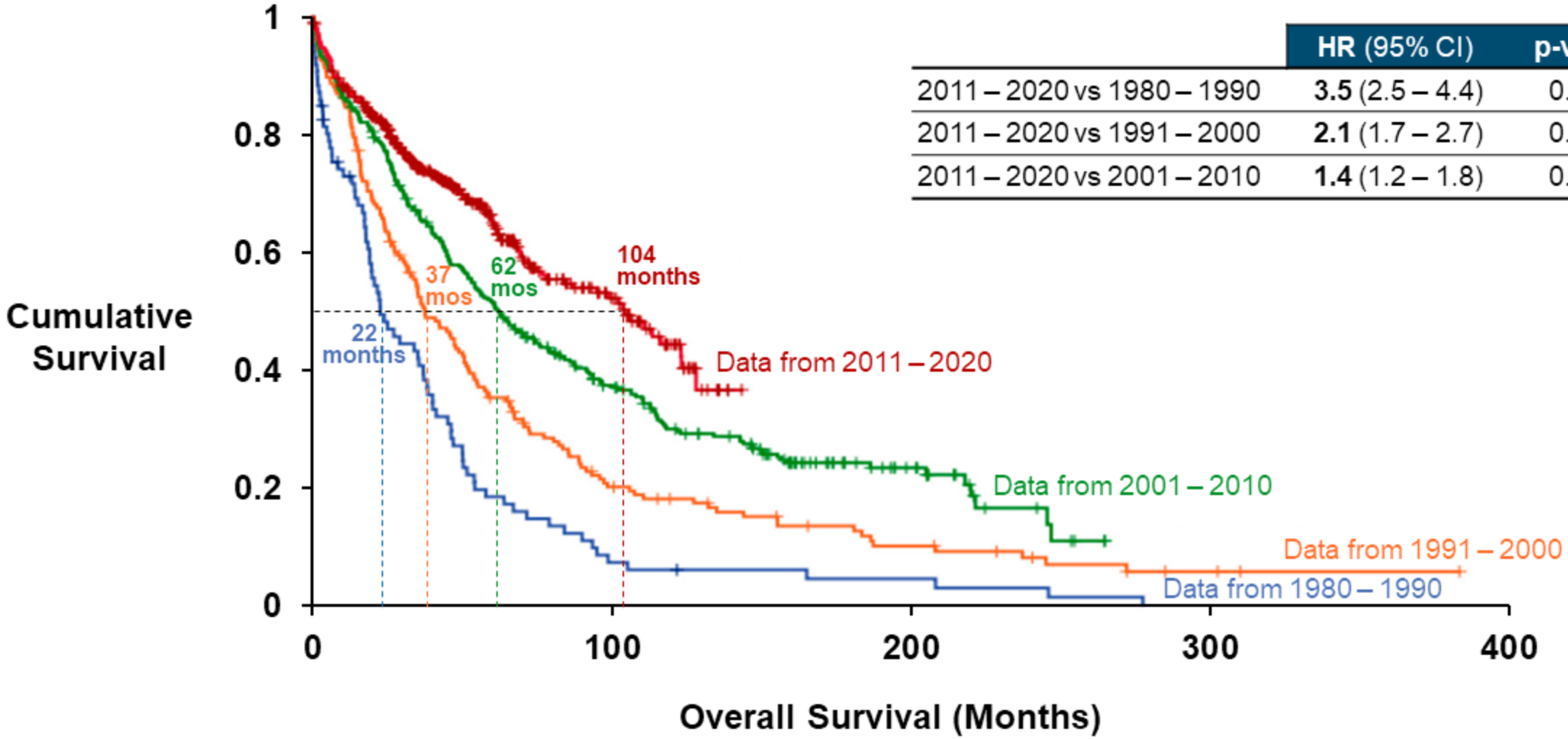
Professor of Medicine

Dana Farber Cancer Institute

Harvard Medical School

Survival has Improved, But Multiple Myeloma Remains an Incurable Disease

	HR (95% CI)	p-value
2011 – 2020 vs 1980 – 1990	**3.5** (2.5 – 4.4)	0.000
2011 – 2020 vs 1991 – 2000	**2.1** (1.7 – 2.7)	0.000
2011 – 2020 vs 2001 – 2010	**1.4** (1.2 – 1.8)	0.001



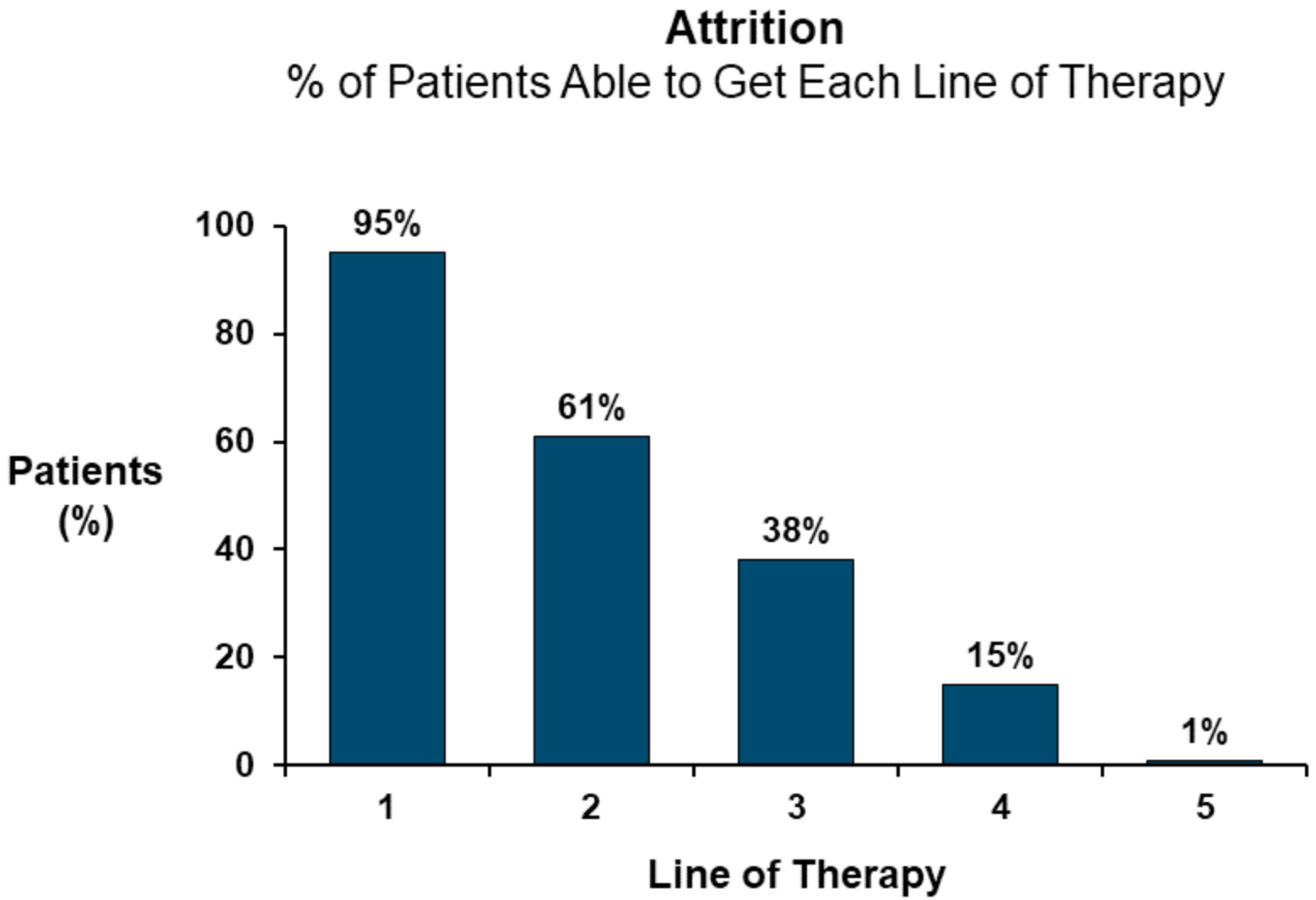
Puertas Cancers, 2023

Why Use CAR-T Therapy Earlier?

- Improved response once MM becomes lenalidomide-refractory
- Patients are lost to attrition with each line of therapy
- Use of T cells in earlier setting, when less exhausted, associated with better long-term outcomes[1]
- Use of CAR-T earlier means less ongoing exposure to burdensome therapy, which is given until disease progression, supporting benefit for patients

1. Haradhvala, 2022

Initial Treatment is Best Chance for Deep and Durable Remissions



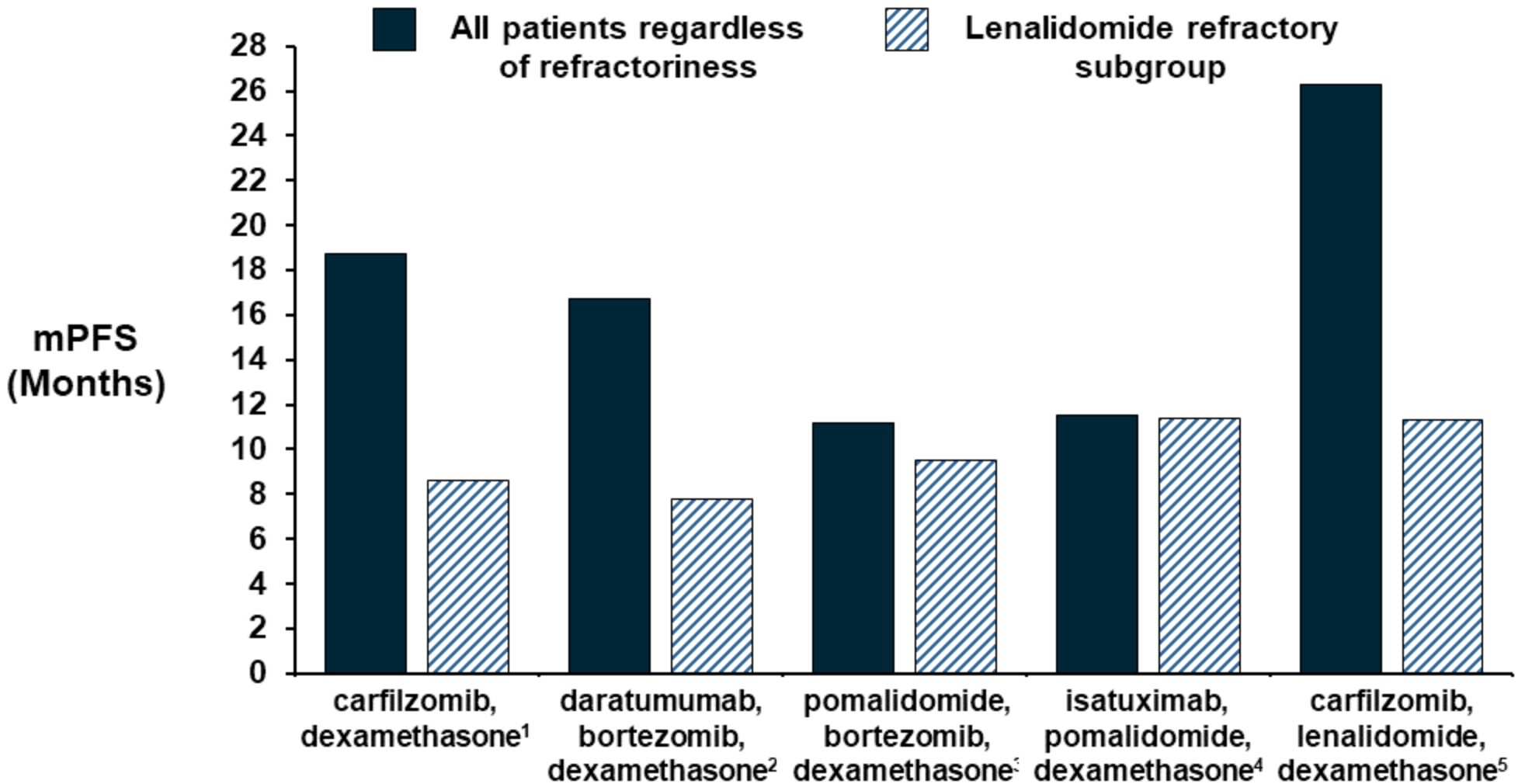
Yong, 2016; Attrition trend consistent with updated data from Dhakal, 2023

T-Cell Exhaustion with Multiple Relapses

- Immune system changes occur during disease progression[1]
  - Significant increase in exhausted T cells with each progression
  - More terminally differentiated T cells at later disease stages
- Developing CAR-T cells from less exhausted T cells is beneficial
  - Naïve-like-central memory T cells that are enriched in earlier disease stage are associated with better clinical response[2]
  - In CARTITUDE-1, longer PFS associated with less exhausted stem-like phenotype CAR cells[3]

1. Haradhvala, 2022; 2. Cohen, 2018; Darcy, 2018; Fraietta, 2018; 3. Montes De Oca et Al, ASH 2023

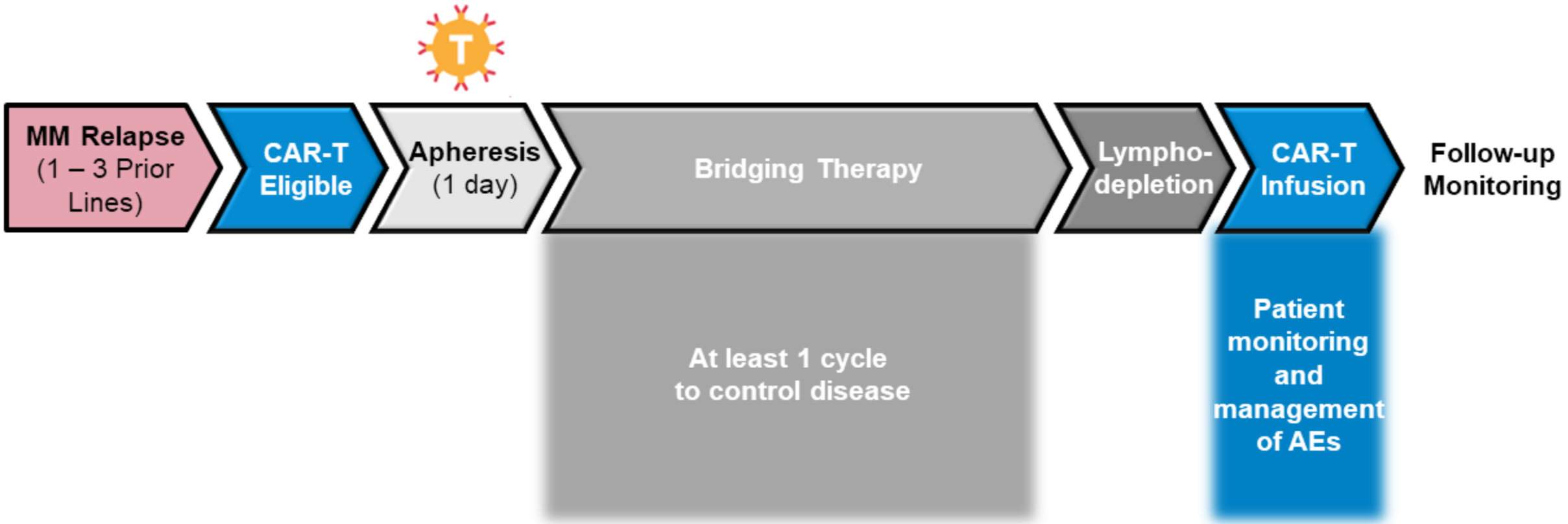
Therapy Effectiveness Diminished Once Patients Become Lenalidomide-Refractory



Data from registrational trials

1. ENDEAVOR, Moreau 2017; 2. CASTOR, Mateos 2020; 3. OPTIMISMM, Richardson 2019; 4. ICARIA, Bringhen 2021; 5. [b] ASPIRE, Dimopoulos 2017

Patient Journey with Cilta-cel in CARTITUDE-4 Study



Summary of Unmet Need

- Significant and critical unmet need for new therapeutic options for lenalidomide-refractory multiple myeloma used earlier in treatment sequence
- Earlier CAR-T therapy offers our patients
  - Deeper remissions
  - Better long-term outcomes
  - One-time infusion

CARTITUDE-4 Efficacy

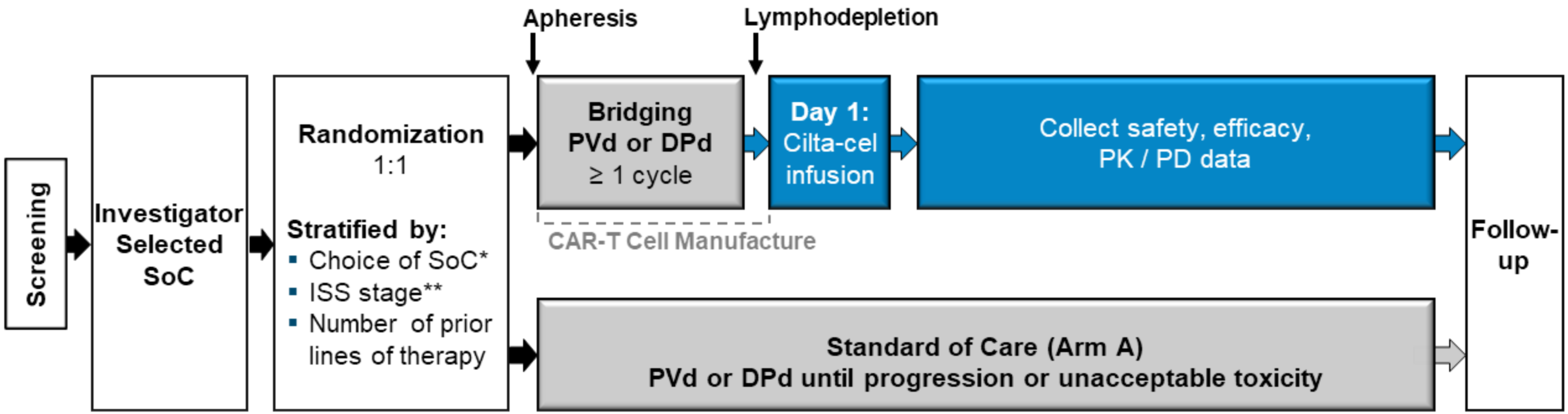
Jordan Schecter, MD

Vice President

Research & Development

Johnson & Johnson Innovative Medicine

CARTITUDE-4: Study Design and Endpoints



*DPd, daratumumab, pomalidomide, and dexamethasone; PVd, pomalidomide, bortezomib, and dexamethasone
**International Staging System (ISS)

CARTITUDE-4: Efficacy Endpoints

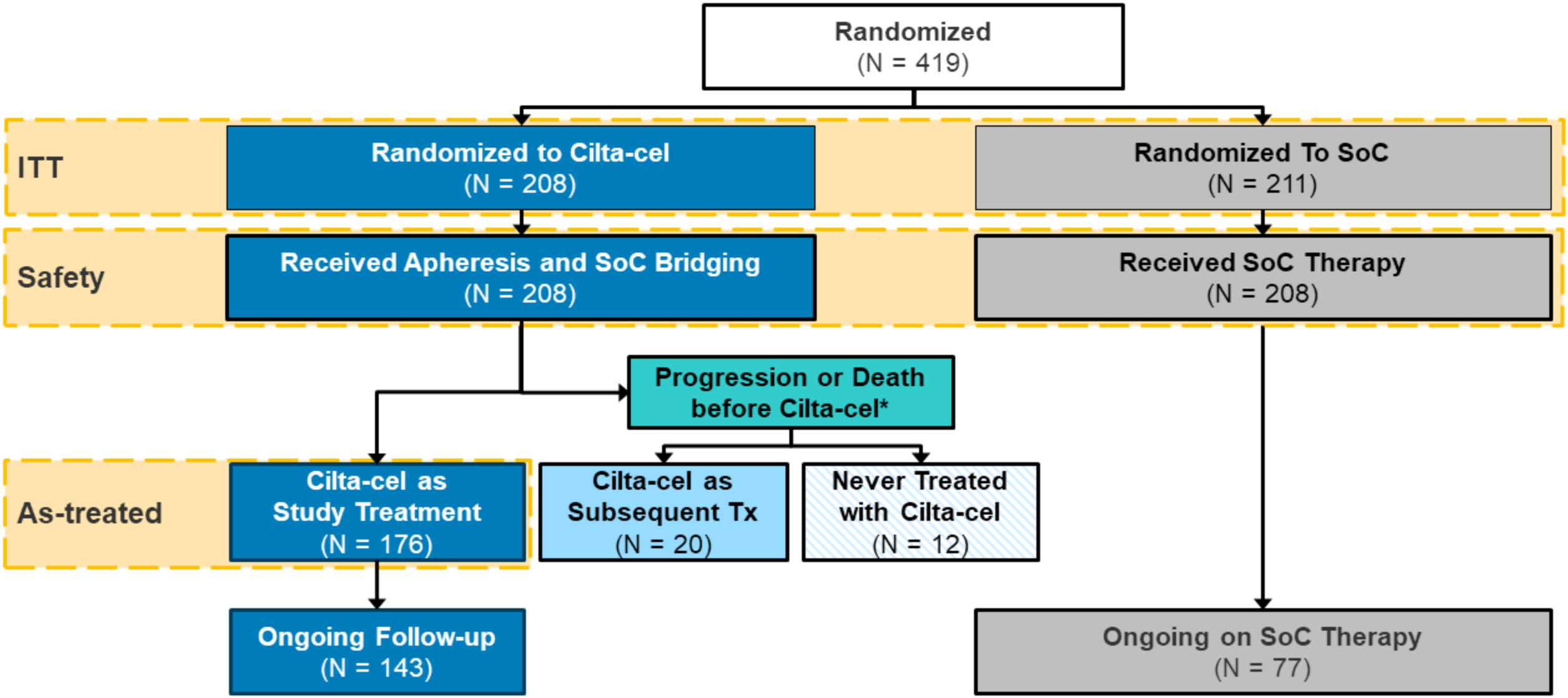
- Primary endpoint: Progression-free survival (PFS)
- Key secondary endpoints
  - sCR / CR
  - ORR
  - MRD negativity
  - OS
- Endpoints assessed by IMWG criteria using computerized algorithm and independent review committee (IRC)

IMWG: International Myeloma Working Group

CARTITUDE-4: Baseline Demographics and Disease Characteristics Balanced Between Arms

	Cilta-cel (N = 208)	Standard of Care (N = 211)
Age, median (range), years	61.5 (27 – 78)	61.0 (35 – 80)
Male	56%	59%
ECOG PS		
0	55%	57%
1/2	45%	43%
ISS stage		
I	65%	63%
II	29%	31%
III	6%	7%
Bone marrow plasma cells ≥ 60%	20%	21%
Presence of soft tissue plasmacytomas	21%	17%
Years since diagnosis, median (range)	3 (0.3 – 18.1)	3.4 (0.4 – 22.1)
Prior lines of therapy, median (range)	2 (1 – 3)	2 (1 – 3)
1 prior line of therapy	33%	32%
2 or 3 prior lines of therapy	67%	68%
Cytogenetic high risk	59%	63%
del(17p)	24%	21%
Lenalidomide-refractory	100%	100%
Anti-CD-38-refractory	24%	22%

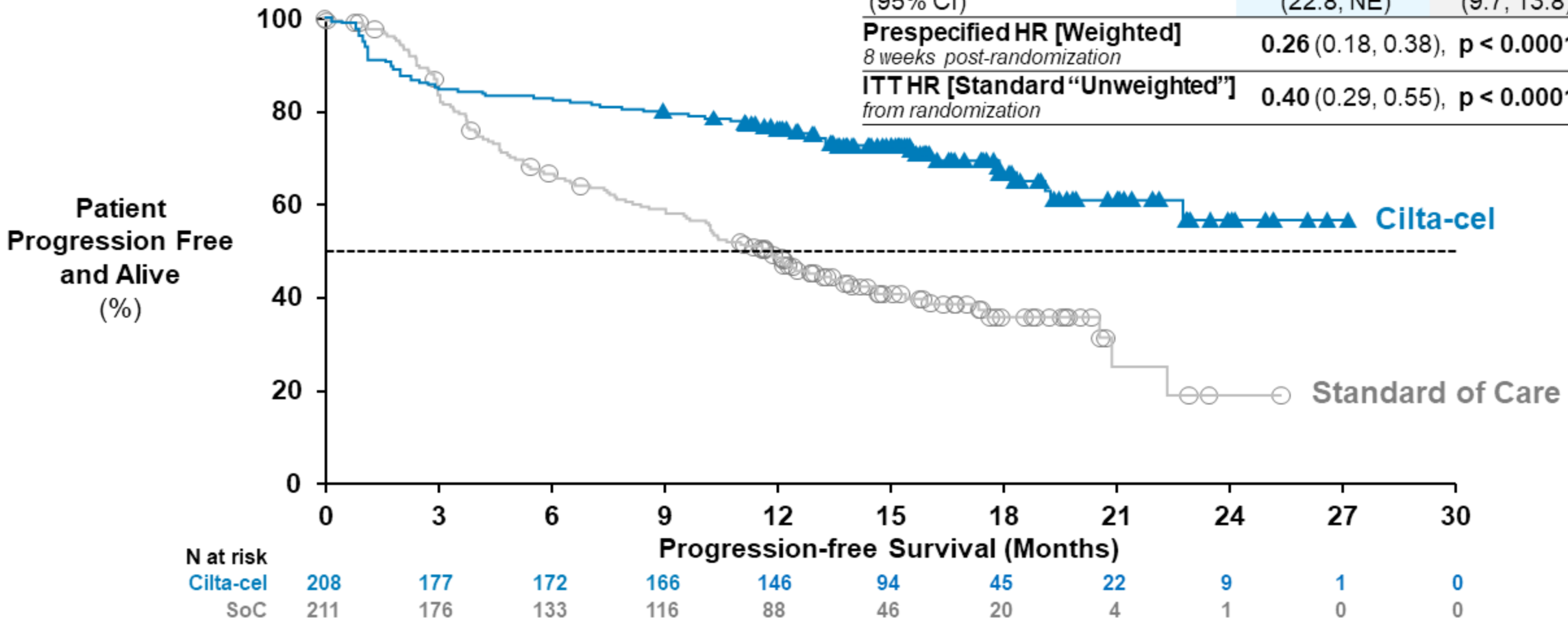
CARTITUDE-4: CONSORT Diagram



*31 patients progressed and 1 died prior to Cilta-cel infusion

CARTITUDE-4: Significant and Meaningful PFS Improvement Compared to SoC

	Cilta-cel (N = 208)	SoC (N = 211)
mPFS, months (95% CI)	**NE** (22.8, NE)	**11.8** (9.7, 13.8)
Prespecified HR [Weighted] *8 weeks post-randomization*	**0.26** (0.18, 0.38),	**p < 0.0001**
ITT HR [Standard "Unweighted"] *from randomization*	**0.40** (0.29, 0.55),	**p < 0.0001**

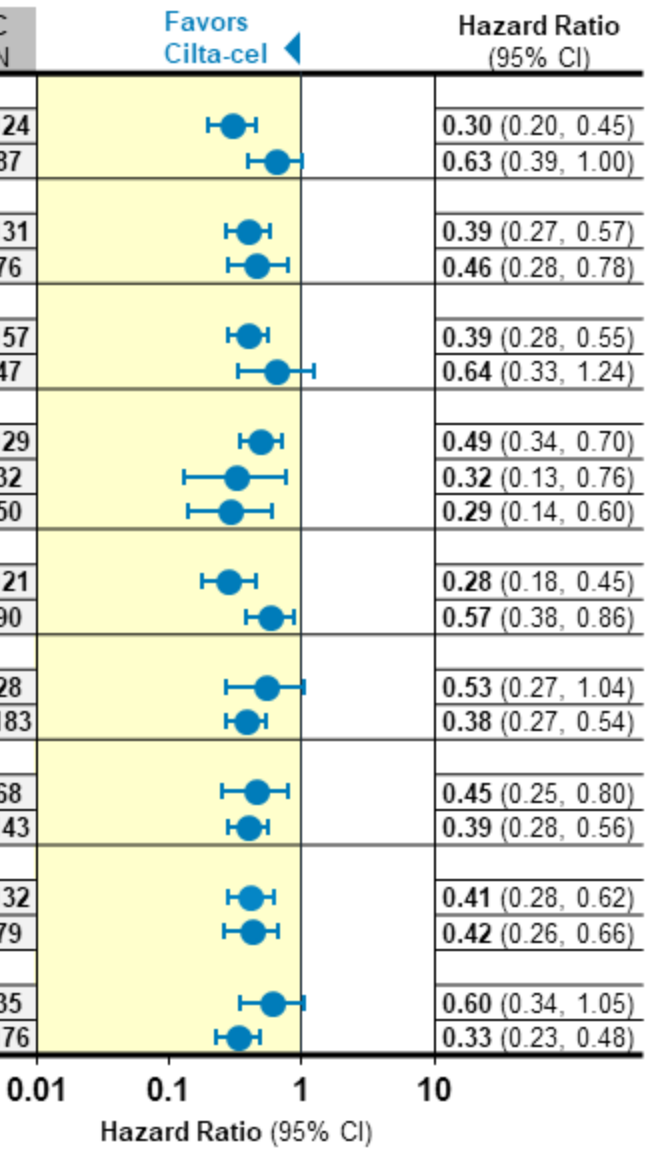


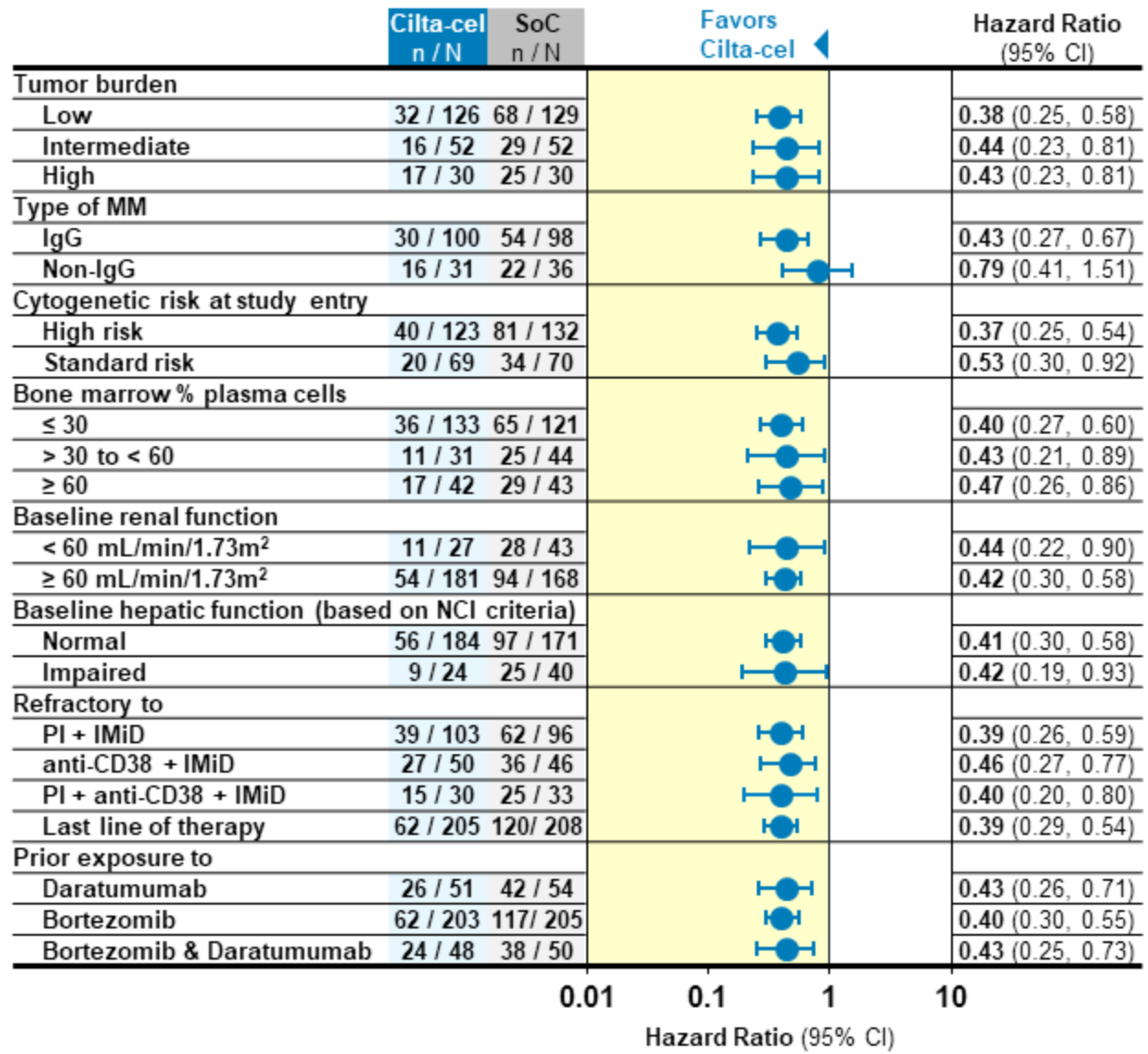
Clinical Cut-Off: 1 November 2022

CARTITUDE-4: Consistent PFS Across Subgroups

	Cilta-cel n / N	SoC n / N	Hazard Ratio (95% CI)
Sex			
Male	34 / 116	80 / 124	0.30 (0.20, 0.45)
Female	31 / 92	42 / 87	0.63 (0.39, 1.00)
Age			
< 65 years	40 / 126	81 / 131	0.39 (0.27, 0.57)
65 – 75 years	25 / 78	39 / 76	0.46 (0.28, 0.78)
Race			
White	50 / 157	94 / 157	0.39 (0.28, 0.55)
Others	15 / 45	22 / 47	0.64 (0.33, 1.24)
Region			
Europe	48 / 128	79 / 129	0.49 (0.34, 0.70)
North America	7 / 32	17 / 32	0.32 (0.13, 0.76)
Other	10 / 48	26 / 50	0.29 (0.14, 0.60)
Baseline ECOG			
0	25 / 114	67 / 121	0.28 (0.18, 0.45)
≥ 1	40 / 94	55 / 90	0.57 (0.38, 0.86)
Investigator's choice of PVd or DPd			
PVd	15 / 26	21 / 28	0.53 (0.27, 1.04)
DPd	50 / 182	101/ 183	0.38 (0.27, 0.54)
Number of lines of prior therapy			
1	18 / 68	33 / 68	0.45 (0.25, 0.80)
2 or 3	47 / 140	89 / 143	0.39 (0.28, 0.56)
ISS staging			
I	36 / 136	67 / 132	0.41 (0.28, 0.62)
II or III	29 / 72	55 / 79	0.42 (0.26, 0.66)
Presence of soft tissue plasmacytomas			
Yes	24 / 44	26 / 35	0.60 (0.34, 1.05)
No	41 / 164	96 / 176	0.33 (0.23, 0.48)

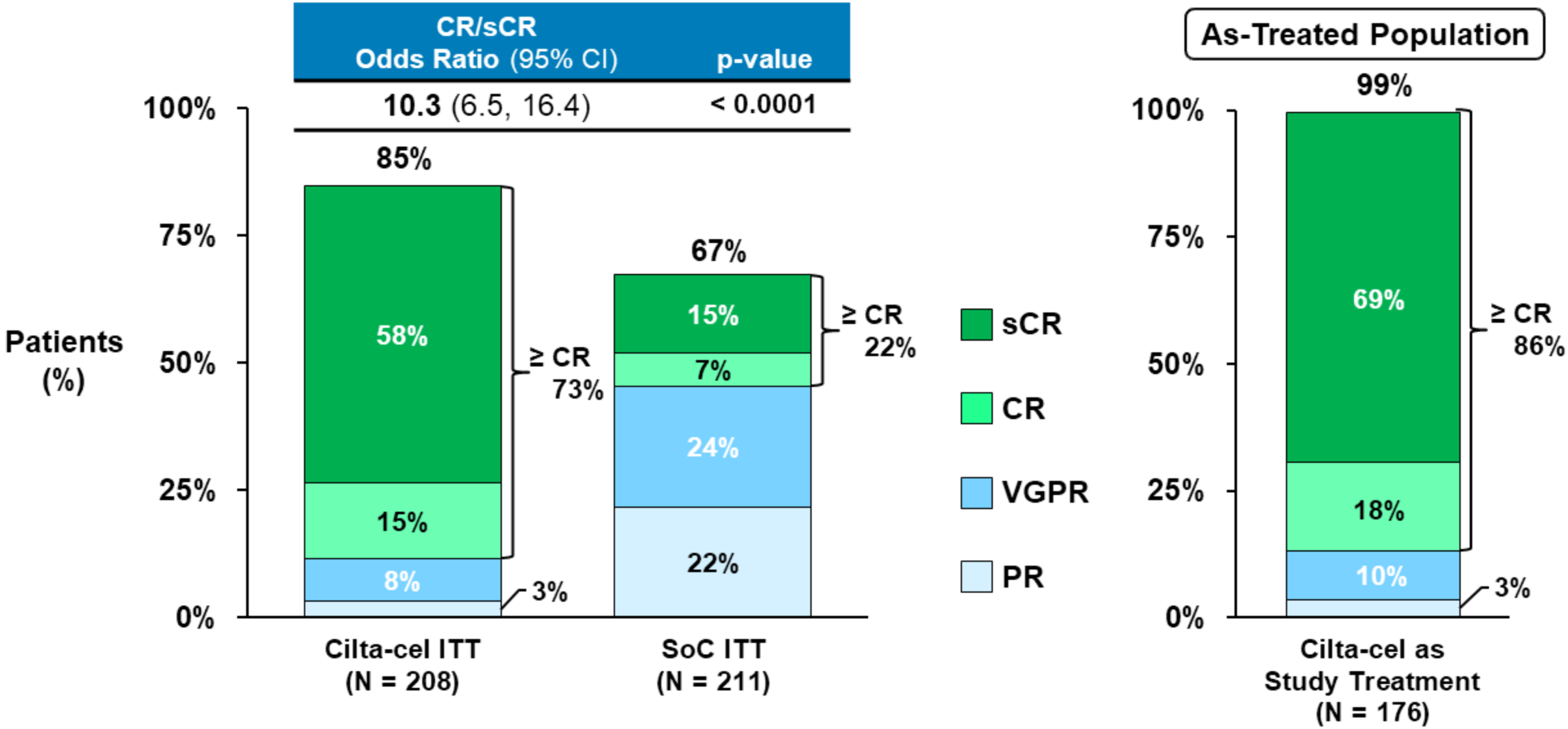
	Cilta-cel n / N	SoC n / N	Hazard Ratio (95% CI)
Tumor burden			
Low	32 / 126	68 / 129	0.38 (0.25, 0.58)
Intermediate	16 / 52	29 / 52	0.44 (0.23, 0.81)
High	17 / 30	25 / 30	0.43 (0.23, 0.81)
Type of MM			
IgG	30 / 100	54 / 98	0.43 (0.27, 0.67)
Non-IgG	16 / 31	22 / 36	0.79 (0.41, 1.51)
Cytogenetic risk at study entry			
High risk	40 / 123	81 / 132	0.37 (0.25, 0.54)
Standard risk	20 / 69	34 / 70	0.53 (0.30, 0.92)
Bone marrow % plasma cells			
≤ 30	36 / 133	65 / 121	0.40 (0.27, 0.60)
> 30 to < 60	11 / 31	25 / 44	0.43 (0.21, 0.89)
≥ 60	17 / 42	29 / 43	0.47 (0.26, 0.86)
Baseline renal function			
< 60 mL/min/1.73m^2	11 / 27	28 / 43	0.44 (0.22, 0.90)
≥ 60 mL/min/1.73m^2	54 / 181	94 / 168	0.42 (0.30, 0.58)
Baseline hepatic function (based on NCI criteria)			
Normal	56 / 184	97 / 171	0.41 (0.30, 0.58)
Impaired	9 / 24	25 / 40	0.42 (0.19, 0.93)
Refractory to			
PI + IMiD	39 / 103	62 / 96	0.39 (0.26, 0.59)
anti-CD38 + IMiD	27 / 50	36 / 46	0.46 (0.27, 0.77)
PI + anti-CD38 + IMiD	15 / 30	25 / 33	0.40 (0.20, 0.80)
Last line of therapy	62 / 205	120/ 208	0.39 (0.29, 0.54)
Prior exposure to			
Daratumumab	26 / 51	42 / 54	0.43 (0.26, 0.71)
Bortezomib	62 / 203	117/ 205	0.40 (0.30, 0.55)
Bortezomib & Daratumumab	24 / 48	38 / 50	0.43 (0.25, 0.73)



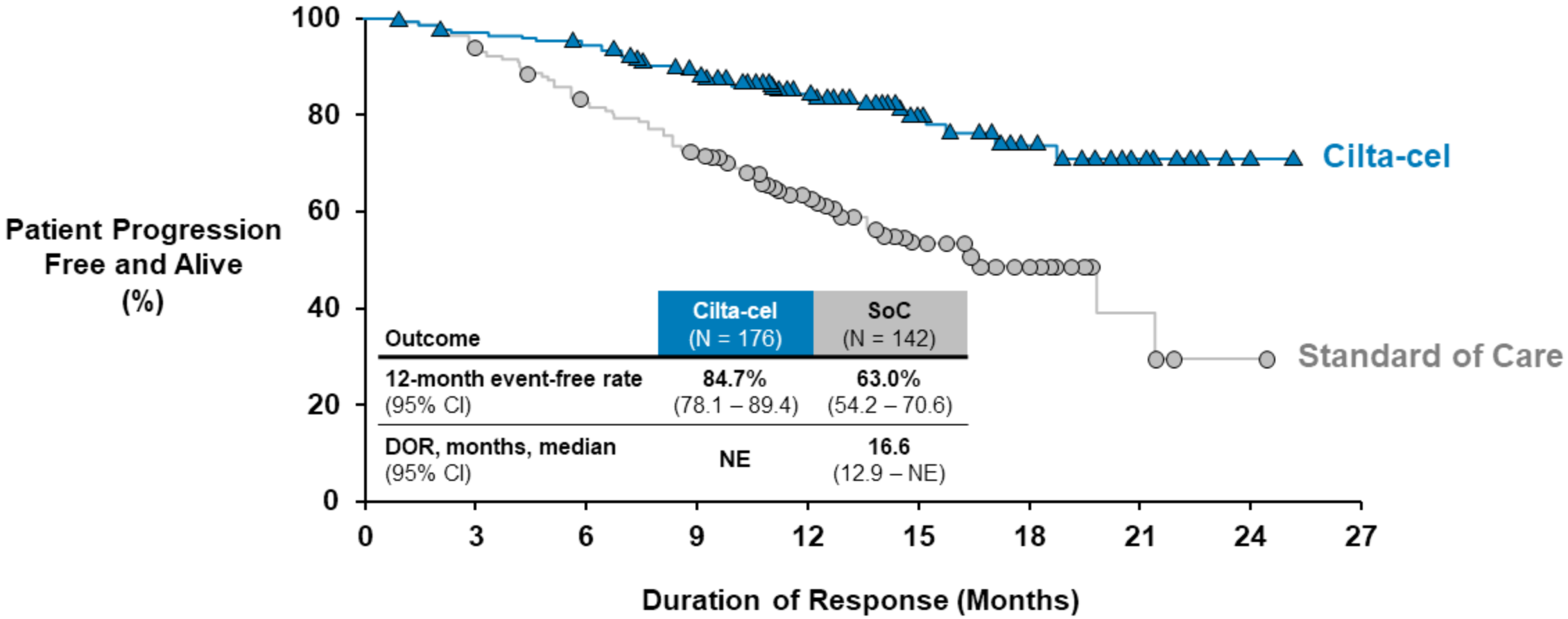


Standard Unweighted

CARTITUDE-4: Single Cilta-cel Infusion Demonstrated Deep and Durable Responses Over SoC



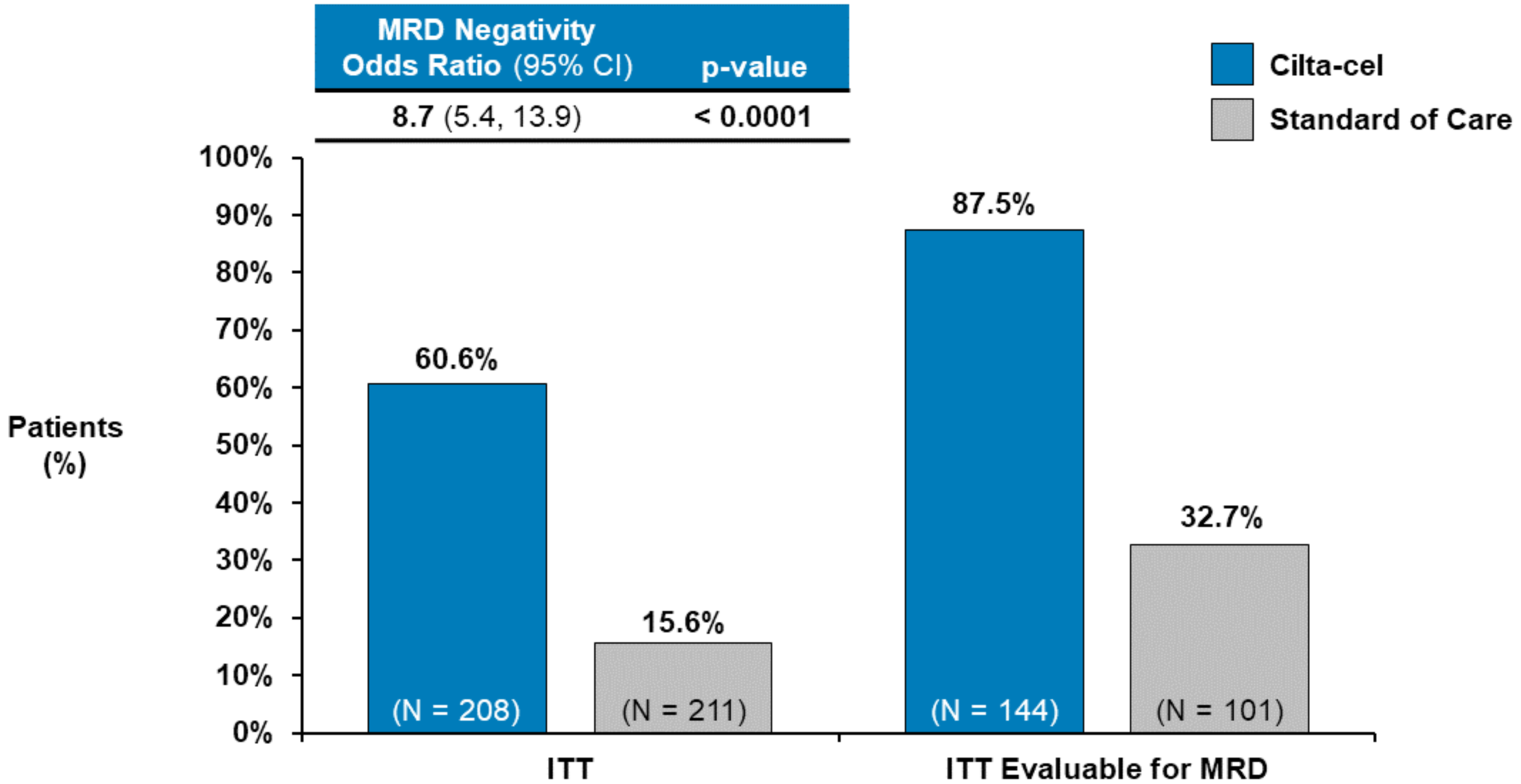
CARTITUDE-4: Secondary Endpoint – Duration of Response (DOR)



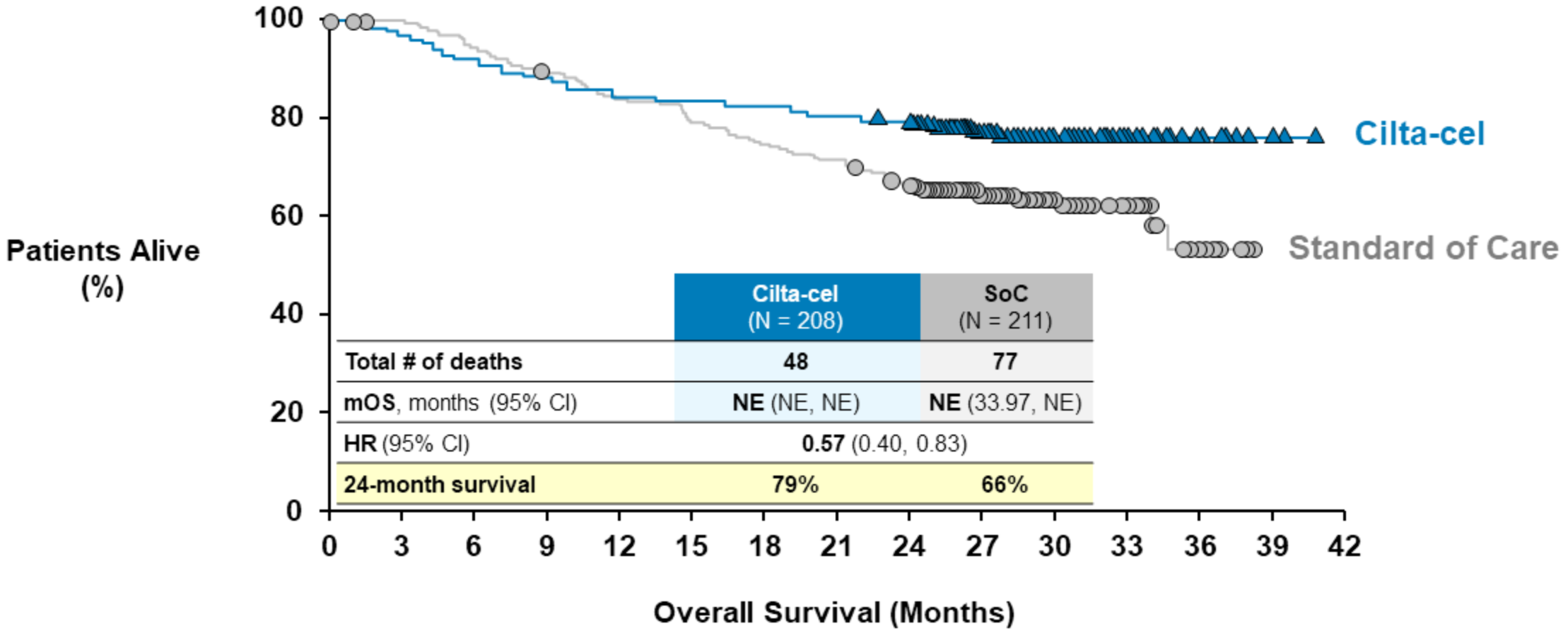
N at risk										
Cilta-cel	176	169	162	143	91	48	27	11	2	0
SoC	142	133	114	99	62	32	14	4	1	0

Clinical Cut-Off: 1 November 2022

CARTITUDE-4: Cilta-cel Improved Rates of Overall MRD Negativity



CARTITUDE-4: OS Strengthens as Data Mature (ITT) December 2023 Data Cut-off

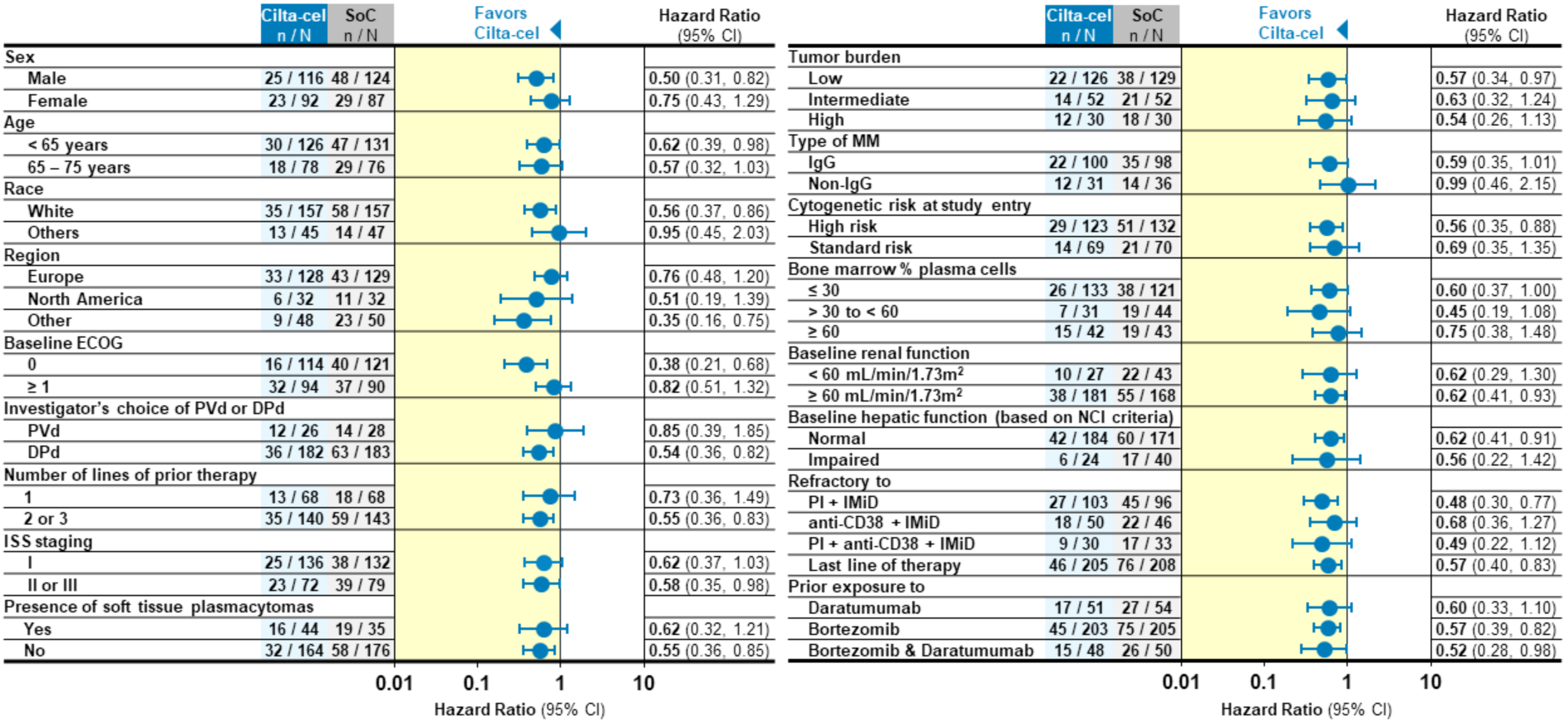


N at risk

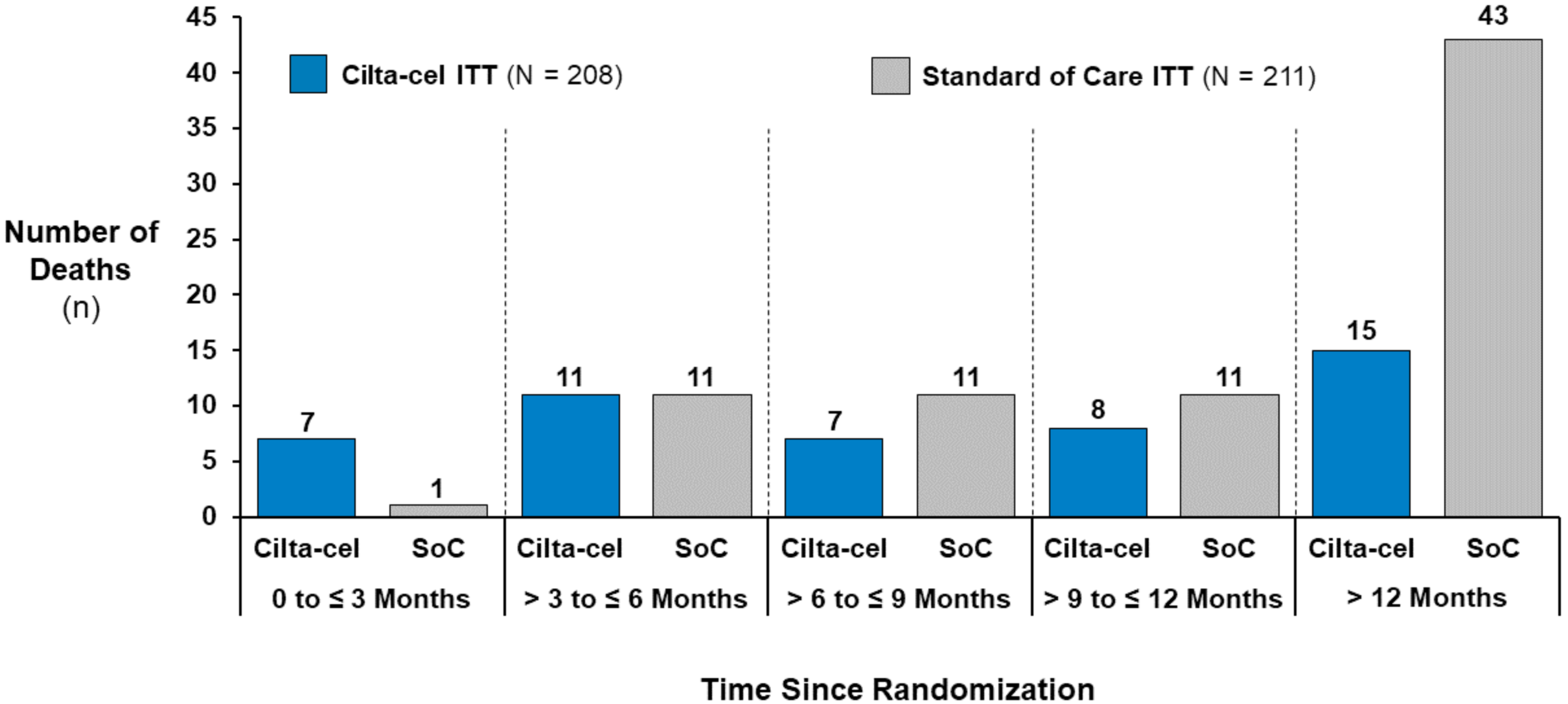
Cilta-cel	208	201	190	183	175	173	171	167	163	109	58	31	12	3	0
SoC	211	207	196	184	173	163	154	147	134	85	44	23	7	0	0

Consistent OS Across Subgroups December 2023 Data Cut-off

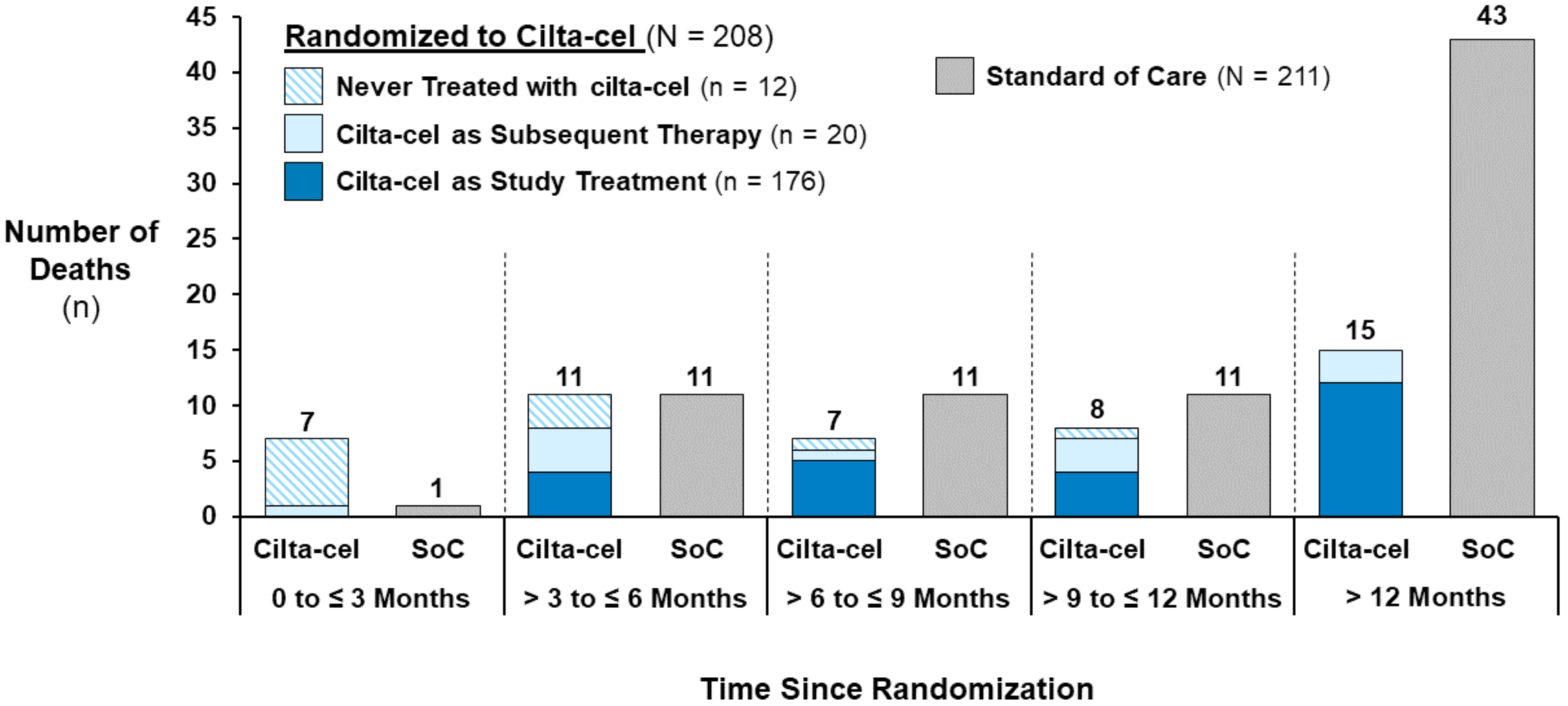
	Cilta-cel n / N	SoC n / N	Hazard Ratio (95% CI)
Sex			
Male	25 / 116	48 / 124	0.50 (0.31, 0.82)
Female	23 / 92	29 / 87	0.75 (0.43, 1.29)
Age			
< 65 years	30 / 126	47 / 131	0.62 (0.39, 0.98)
65 – 75 years	18 / 78	29 / 76	0.57 (0.32, 1.03)
Race			
White	35 / 157	58 / 157	0.56 (0.37, 0.86)
Others	13 / 45	14 / 47	0.95 (0.45, 2.03)
Region			
Europe	33 / 128	43 / 129	0.76 (0.48, 1.20)
North America	6 / 32	11 / 32	0.51 (0.19, 1.39)
Other	9 / 48	23 / 50	0.35 (0.16, 0.75)
Baseline ECOG			
0	16 / 114	40 / 121	0.38 (0.21, 0.68)
≥ 1	32 / 94	37 / 90	0.82 (0.51, 1.32)
Investigator's choice of PVd or DPd			
PVd	12 / 26	14 / 28	0.85 (0.39, 1.85)
DPd	36 / 182	63 / 183	0.54 (0.36, 0.82)
Number of lines of prior therapy			
1	13 / 68	18 / 68	0.73 (0.36, 1.49)
2 or 3	35 / 140	59 / 143	0.55 (0.36, 0.83)
ISS staging			
I	25 / 136	38 / 132	0.62 (0.37, 1.03)
II or III	23 / 72	39 / 79	0.58 (0.35, 0.98)
Presence of soft tissue plasmacytomas			
Yes	16 / 44	19 / 35	0.62 (0.32, 1.21)
No	32 / 164	58 / 176	0.55 (0.36, 0.85)
Tumor burden			
Low	22 / 126	38 / 129	0.57 (0.34, 0.97)
Intermediate	14 / 52	21 / 52	0.63 (0.32, 1.24)
High	12 / 30	18 / 30	0.54 (0.26, 1.13)
Type of MM			
IgG	22 / 100	35 / 98	0.59 (0.35, 1.01)
Non-IgG	12 / 31	14 / 36	0.99 (0.46, 2.15)
Cytogenetic risk at study entry			
High risk	29 / 123	51 / 132	0.56 (0.35, 0.88)
Standard risk	14 / 69	21 / 70	0.69 (0.35, 1.35)
Bone marrow % plasma cells			
≤ 30	26 / 133	38 / 121	0.60 (0.37, 1.00)
> 30 to < 60	7 / 31	19 / 44	0.45 (0.19, 1.08)
≥ 60	15 / 42	19 / 43	0.75 (0.38, 1.48)
Baseline renal function			
< 60 mL/min/1.73m^2	10 / 27	22 / 43	0.62 (0.29, 1.30)
≥ 60 mL/min/1.73m^2	38 / 181	55 / 168	0.62 (0.41, 0.93)
Baseline hepatic function (based on NCI criteria)			
Normal	42 / 184	60 / 171	0.62 (0.41, 0.91)
Impaired	6 / 24	17 / 40	0.56 (0.22, 1.42)
Refractory to			
PI + IMiD	27 / 103	45 / 96	0.48 (0.30, 0.77)
anti-CD38 + IMiD	18 / 50	22 / 46	0.68 (0.36, 1.27)
PI + anti-CD38 + IMiD	9 / 30	17 / 33	0.49 (0.22, 1.12)
Last line of therapy	46 / 205	76 / 208	0.57 (0.40, 0.83)
Prior exposure to			
Daratumumab	17 / 51	27 / 54	0.60 (0.33, 1.10)
Bortezomib	45 / 203	75 / 205	0.57 (0.39, 0.82)
Bortezomib & Daratumumab	15 / 48	26 / 50	0.52 (0.28, 0.98)



CARTITUDE-4: OS Imbalance Due to Progression or Death Prior to Cilta-cel Infusion in Cilta-cel Arm



CARTITUDE-4: OS Imbalance Due to Progression or Death Prior to Cilta-cel Infusion in Cilta-cel Arm



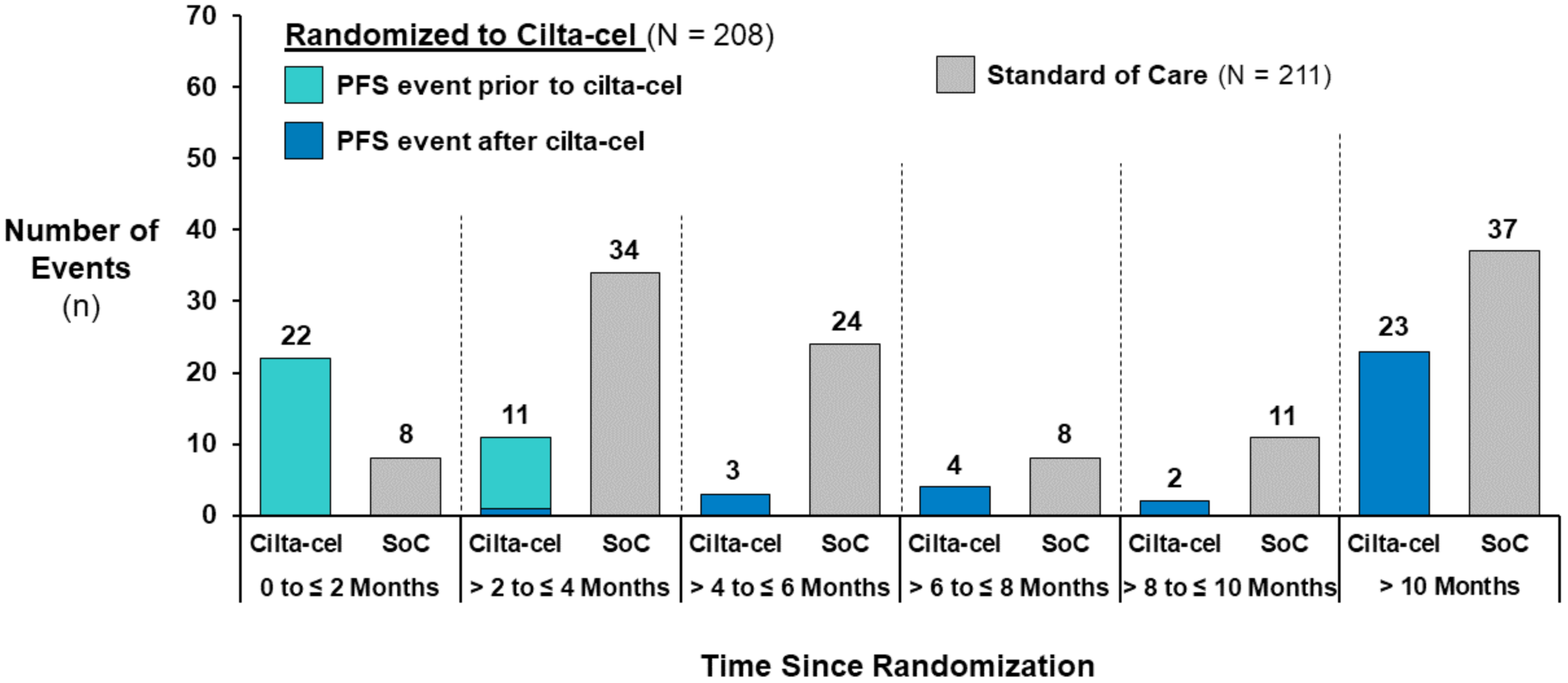
CARTITUDE-4: Early Deaths in Cilta-cel Arm Primarily in Patients with Progression Before Cilta-cel Infusion

Cause of Death	0 - ≤ 3 Months				> 3 - ≤ 6 Months			
	Never Treated with Cilta-cel (n = 12)	Cilta-cel as Subsequent Therapy (n = 20)	Cilta-cel as Study Treatment (n = 176)	SoC (N = 211)	Never Treated with Cilta-cel (n = 12)	Cilta-cel as Subsequent Therapy (n = 20)	Cilta-cel as Study Treatment (n = 176)	SoC (N = 211)
Total Deaths	6	1	0	1	3	4	4	11
Progressive disease	4	-	-	1	3	-	1	5
AEs	2	1	-	-	-	4	3*	6

** All COVID-19 pneumonia*

Deaths presented are from randomization

CARTITUDE-4: PFS Imbalance Occurs Early in Patients Who Did Not Receive Cilta-cel as Study Treatment



Comprehensive Analyses to Assess Imbalance in Early Progression Events

- Parameters assessed for potential association with early PFS
  - Demographics and baseline disease characteristics
    - Including known risk factors for early progression
  - Study related factors such as apheresis procedure
  - CAR-T manufacturing time
  - Bridging therapy (starting time and dose intensity)
  - Exposure to lymphodepletion
- Lower relative dose intensity of bridging therapy may have contributed to imbalance

Investigations for Early PFS Events

: Investigations did not identify these factors as major contributors to the early imbalance in PFS events

Difference in Relative Dose Intensity of Bridging Therapy

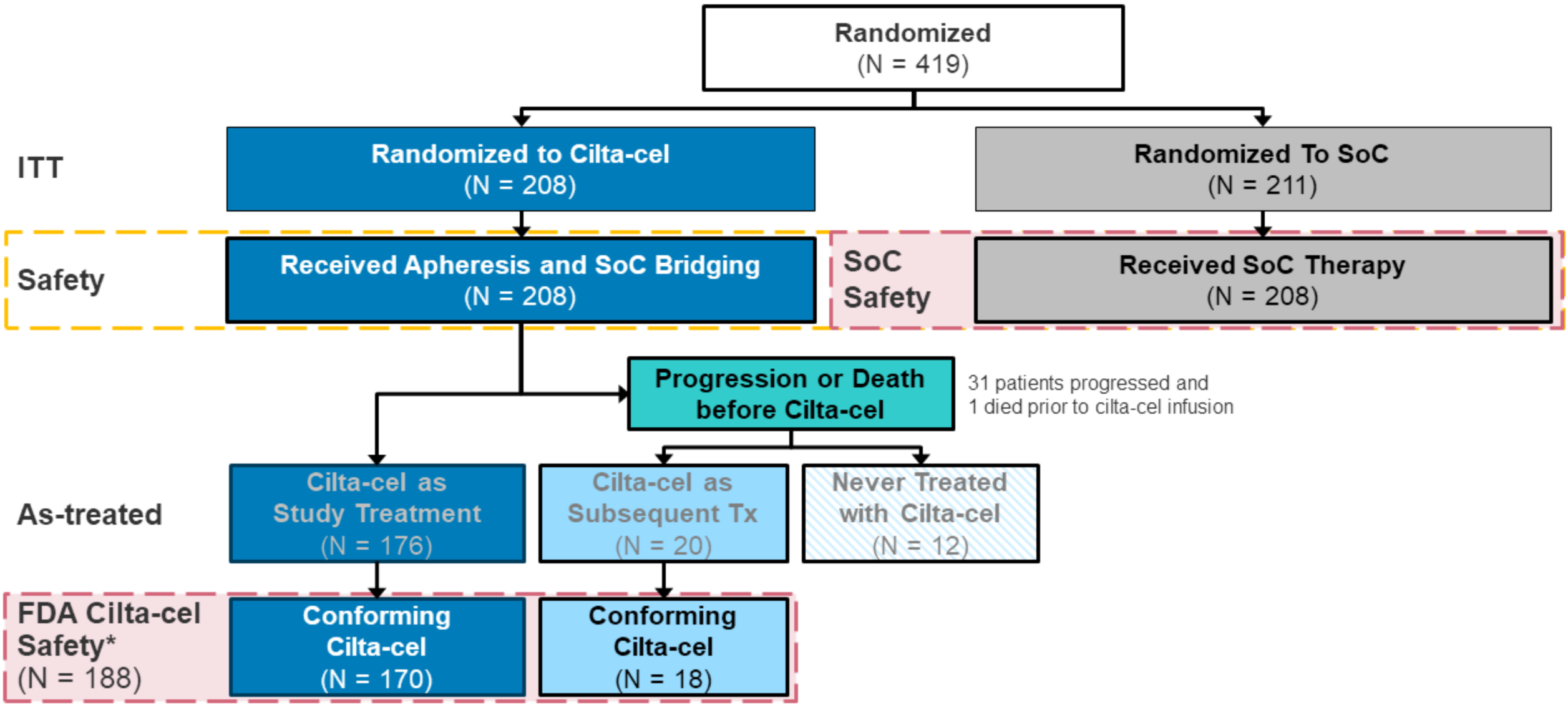
	Cilta-cel (N = 208)	Standard of Care (N = 208)
Pomalidomide	207	208
Median	**81.0%**	**94.5%**
Bortezomib	26	26
Median	**73.2%**	**87.5%**
Dexamethasone	207	208
Median	**88.9%**	**90.0%**
Daratumumab	181	182
Median	**81.3%**	**80.0%**

Cilta-cel Demonstrated Statistically Significant and Clinically Meaningful Improvement for Patients with RRMM (1 – 3 Lines)

- PFS: HR (95% CI) = 0.40 (0.29, 0.55)
  - 12-month PFS rate 76% in cilta-cel vs 49% in SoC
- ORR: 85% vs 67%
  - CR / sCR = 73% vs 22%
  - MRD negativity = 61% vs 16%
- OS continues to strengthen as data mature
- Results consistent across subgroups

CARTITUDE-4: Clinical Safety

FDA Safety Analysis Set Uses Patients Who Received Conforming Cilta-cel



*Cilta-cel post-infusion events (excludes AEs from bridging therapy and lymphodepletion following randomization and until cilta-cel infusion)

CARTITUDE-4: Safety Profile Similar Between Arms

Adverse Events	Safety Population	
	Cilta-cel* (N = 188)	Standard of Care (N = 208)
Any AE	100%	100%
Max Grade 3 – 4**	84%	91%
Non-fatal serious AE	35%	38%
AE Leading to Death (Nov 2022 Data Cut-off)	11%	8%
AE Leading to Death (Dec 2023 Data Cut-off)	12%	13%

November 2022 Interim Analysis Data Cut-off unless specified

*Cilta-cel post-infusion events; **Patients with G3-4 events that subsequently died of similar Grade 5 event included in AE leading to death

CARTITUDE-4: AEs as Cause of Death
December 2023 Data Cut-off

	Cilta-cel* (n = 188)	Standard of Care (N = 208)
Any AE Leading to Death	12%	13%
Hemorrhage	2%	1%
Pneumonia	5%	2%
COVID-19 pneumonia	4%	1%
Sepsis	2%	2%
Viral infection	0.5%	2%
COVID-19	0	1%
Upper respiratory tract infection	0	1%
Acute interstitial pneumonitis	0	0.5%
Multi-Organ failure	0.5%	1%
Renal failure	0	1%
AML / MDS	2%	0

* Cilta-cel post-infusion events

Cilta-cel Common Adverse Events Align with Approved Label and CAR-T Mechanism of Action

Adverse Events ≥ 30%	Cilta-cel* (N = 188)	Standard of Care (N = 208)
Any AE	100%	100%
Neutropenia	84%	85%
Cytokine release syndrome (CRS)	78%	0.5%
Thrombocytopenia	48%	31%
Anemia	48%	26%
Hypogammaglobulinemia	48%	6%
Musculoskeletal pain	34%	47%
Fatigue	28%	50%
Upper respiratory tract infection	25%	40%
Viral infection	23%	31%

* Cilta-cel post-infusion events

AEs Grade 3 – 4

Adverse Events ≥ 5%	Cilta-cel* (N = 188)	Standard of Care (N = 208)
Any AE Grade 3 – 4	92%	94%
Neutropenia	84%	82%
Thrombocytopenia	38%	19%
Anemia	32%	14%
Lymphopenia	20%	12%
Leukopenia	11%	5%
Hypogammaglobulinaemia	9%	0.5%
Pneumonia	9%	11%
Bacterial infection	6%	4%
Sepsis	6%	0.5%
Viral infection	4%	6%
Upper respiratory infection	1%	5%

* Cilta-cel post-infusion events

Serious Adverse Events

Adverse Events ≥ 2%	Cilta-cel* (N = 188)	Standard of Care (N = 208)
Any serious AE	38%	39%
Pneumonia	9%	12%
Viral infection	6%	6%
Cytokine release syndrome	6%	0.5%
Cranial nerve palsies	5%	0.5%
Sepsis	4%	1%
Bacterial infection	2%	3%
Diarrhea	2%	0
Encephalopathy	2%	1%
Gastroenteritis	2%	0.5%
Neutropenia	2%	0.5%
Upper respiratory tract infection	2%	4%
Thrombosis	0.5%	2%
Pyrexia	0.5%	2%
Febrile neutropenia	0	2%

*Cilta-cel post-infusion events

Adverse Events of Special Interest (AESI)

Established Cilta-cel Safety Profile Seen in CARTITUDE-4

	Conforming Cilta-cel As-treated Patients* (N = 188)				
CART-specific AEs	Any Grade	Grade 3 – 4	Median Time to Onset (days)	Median Duration (days)	Resolved (%)
CRS	78%	3%	8	3	99%
ICANS	7%	0.5%	9	2	93%
Cranial nerve palsy	9%	1%	21	77	88%
Peripheral neuropathy	7%	0.5%	51	168	57%
MNT (Parkinsonism)	1%	0	60	265	Ongoing at Clinical Cut-off

*Cilta-cel post-infusion events

CRS = Cytokine release syndrome; ICANS = Immune Effector Cell-Associated Neurotoxicity Syndrome; MNT = Movement and Neurocognitive Toxicity

Second Primary Malignancies

	Cilta-cel* (N = 188)	Standard of Care (N = 208)
Patients with second primary malignancies	9%	8%
Cutaneous / non-invasive malignancies	5%	6%
Hematologic malignancies	3%	0
AML / MDS	2%	0
TCL	0.5%	0
Non-cutaneous / invasive	2%	2%

April 2023 120-Day Safety Update; *Cilta-cel post-infusion events

Safety Profile in Patients Treated with Cilta-cel as Subsequent Therapy

SAE Risk Greater in Patients that Received Cilta-cel as Subsequent Treatment Post Progression

Adverse Events	Cilta-cel (N = 188)		Standard of Care (N = 208)
	Cilta-cel as Study Treatment* (N = 170)	Cilta-cel as Subsequent Tx* (N = 18)	
Any AE	100%	100%	100%
Max Grade 3 – 4	86%	67%	91%
Non-fatal serious AE	33%	56%	38%
AE Leading to Death (Nov 2022 Data Cut-off)	9%	28%	8%
AE Leading to Death (Dec 2023 Data Cut-off)	11%	28%	13%

November 2022 Interim Analysis Data Cut-off unless specified

*Cilta-cel post-infusion events; ** Subjects with G3-4 events that subsequently died of similar Grade 5 event are included in AE leading to death

CARTITUDE-4: AEs as Cause of Death
December 2023 Data Cut-off

	Cilta-cel as Study Treatment* (n = 170)	Cilta-cel as Subsequent Therapy* (n = 18)
Any AE Leading to Death	11%	28%
Hemorrhage	1%	11%
Pneumonia	5%	0
COVID-19 pneumonia	4%	0
Sepsis	1%	11%
Viral infection	1%	0
Multi-Organ failure	1%	0
Cardio-respiratory arrest	0	6%
AML / MDS	2%	0
Plasma cell myeloma	1%	0

* Cilta-cel post-infusion events

Comparison of AESIs for Patients Who Received Conforming Cilta-cel as Study Treatment vs. Subsequent Therapy

	Cilta-cel as Study Treatment* (N = 170)		Cilta-cel as Subsequent Therapy* (N = 18)	
CART-specific AEs	Any Grade	Grade 3 – 4	Any Grade	Grade 3 – 4
CRS	76%	1%	89%	22%
ICANS	5%	0	33%	6%
Cranial nerve palsy	9%	1%	0%	0
Peripheral neuropathy	7%	1%	11%	0
MNT (Parkinsonism)	0.6%	0	6%	0

MNT = Movement and Neurocognitive Toxicity

*Cilta-cel post-infusion events

Summary of Safety

- Safety from CARTITUDE-4 consistent with previous cilta-cel experience and mechanism of CAR-Ts
- Findings suggest reduction in rate and severity of cilta-cel specific AEs in earlier disease setting

Clinical Perspective

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Director of Center of Excellence for Multiple Myeloma
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CARTITUDE-4: Overall Efficacy Perspective

- Overall data outstanding
  - Clinically meaningful PFS improvement
  - Trend towards improved OS
  - MRD negativity 88% in evaluable patients
  - Consistent PFS across subgroups
- Data do not support exclusion of any specific patients
- Imbalance in early progressions mostly in patients who did not receive cilta-cel

Cilta-cel has Achieved Response Unattainable with Other Treatments

Study	% Lenalidomide-refractory	mPFS (Months)	MRD
CARTITUDE-4 (ITT)	100%	NE (95% CI: 22.8, NE)	61%
ICARIA[1] (IsaPd)	94%	11.5	5%
APOLLO[2] (DaraPd)	79%	12.4	9%
OPTIMISMM[3] (PVd)	71%	11.2	N/A
CANDOR[4] (DaraKd)	32%	28.4	28%
IKEMA[5] (IsaKd)	32%	35.7	34%

- Lenalidomide is a key backbone but most patients will become lenalidomide-refractory
- Median PFS in lenalidomide-refractory RRMM is < 12 months[6]
- Regimens based on continuous therapy until progression have cumulative toxicity and treatment burden

1. Attal, 2019 (Isatuximab, pomalidomide and low-dose dexamethasone); 2. Dimopoulos, 2021 (Pomalidomide, Dexamethasone and Daratumumab); 3. Richardson, 2019 (Pomalidomide, bortezomib, and dexamethasone); 4. Usmani, 2023 (carfilzomib, dexamethasone, and daratumumab); 5. Martin, 2023 (Isatuximab, carfilzomib, dexamethasone); 6. de Arriba de la Fuente F, Cancers 2023

Safety Profile: Benefit Clearly Outweighs Well-Known and Manageable Risk

- CRS, ICANS
  - Mostly mild / resolved with standard CAR-T management
  - Other Neurotoxicity events mostly mild
- Infections
  - COVID-19 and risk is now minimized
  - Cytopenias mostly grade 3 and resolved to grade ≤ 2 by day 30

Comparison of CARTITUDE-4 with CARTITUDE-1

CART-specific AEs	Cilta-cel as Study Treatment CARTITUDE-4 (N = 188)		Cilta-cel as Study Treatment CARTITUDE-1 (N = 97)	
	Any Grade	Grade 3 – 4	Any Grade	Grade 3 – 4*
CRS	78%	3%	95%	5%
ICANS	7%	0.5%	23%	3%
Cranial nerve palsy	9%	1%	3%	1%
Peripheral neuropathy	7%	0.5%	7%	2%
MNT (Parkinsonism)	1%	0	6%	4%

*Count excludes: Grade 5 : CRS=1%, ICANS=2%, MNT=1%

Cilta-cel Safety in Context of Other Approved Treatments for RRMM (1 – 3 Prior Lines)

Study	SAEs	AEs Leading to Discontinuations
CARTITUDE-4 (N=188)	38%	N/A since one-time infusion
ICARIA[1] (IsaPd)	62%	7%
APOLLO[2] (DaraPd)	50%	2%
OPTIMISMM[3] (PVd)	57%	11%[6]
CANDOR[4] (DaraKd)	56%	22%
IKEMA[5] (IsaKd)	59%	8%

1. Attal Lancet 2019 (isatuximab, pomalidomide and low-dose dexamethasone); 2. Dimopoulos Lancet Oncol 2021 (pomalidomide, dexamethasone and daratumumab); 3. Richardson Lancet Oncol 2019 (pomalidomide, bortezomib, and dexamethasone); 4. Dimopoulos Lancet 2020 (carfilzomib, dexamethasone, and daratumumab); 5. Moreau Lancet 2021 (isatuximab, carfilzomib, dexamethasone); 6. Richardson ASCO 2018 Abstract 8001

CARVYKTI Provides Significant Clinical Benefit and Would be Invaluable for Lenalidomide-Refractory MM

- Demographics and baseline characteristics balanced
- Subgroup data for PFS and OS consistently favor cilta-cel
  - Including high-risk populations
- AEs appear consistent with known safety of cilta-cel, which is understood and manageable
- Improving bridging therapy to control disease prior to cilta-cel
- Positive benefit-risk for patients with lenalidomide-refractory multiple myeloma

CARVYKTI® (Cilta-cel) for the Treatment of Relapsed and Lenalidomide-Refractory Multiple Myeloma

March 15, 2024

Oncologic Drugs Advisory Committee

Johnson & Johnson Innovative Medicine

Janssen Clarifying Questions and Answers

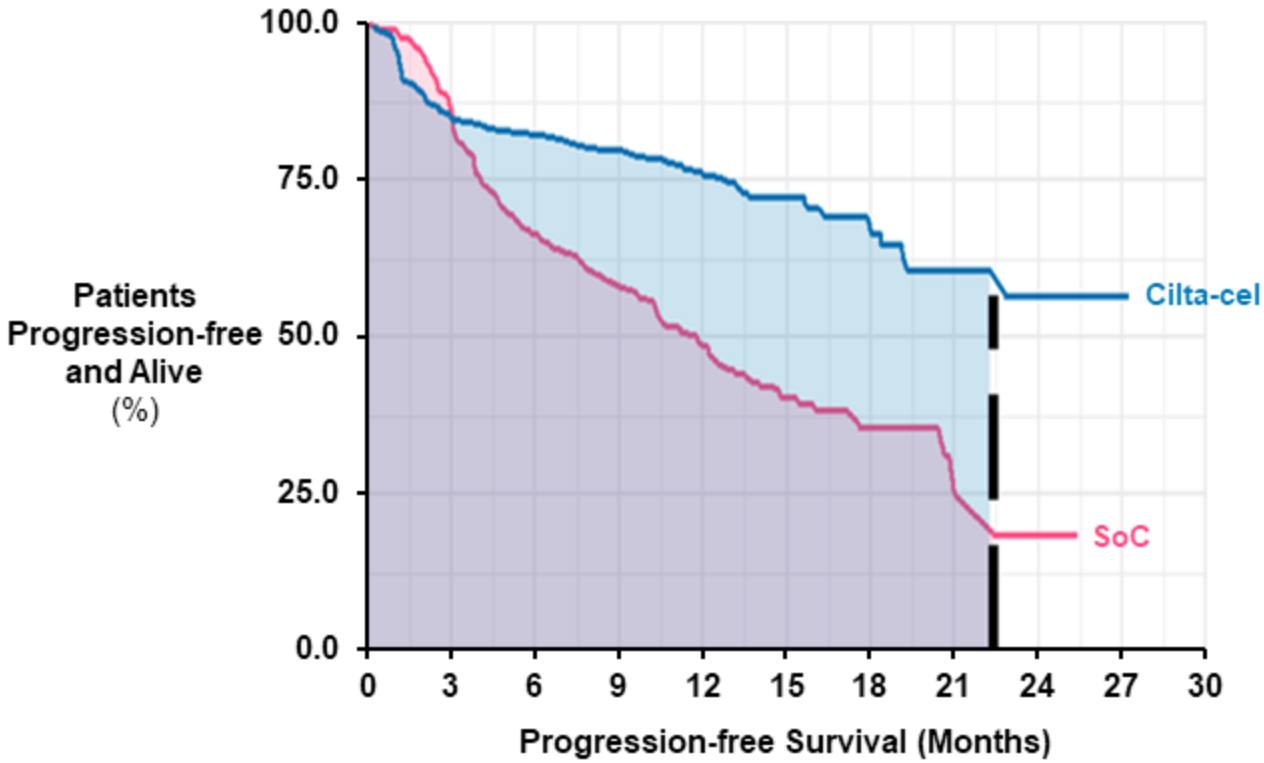
March 15, 2024

CARVYKTI® (Cilta-cel) for the Treatment of Relapsed and Lenalidomide-Refractory Multiple Myeloma

All Non-core Slides Shown During Q&A

Pre-specified Sensitivity Analysis of PFS: RMST

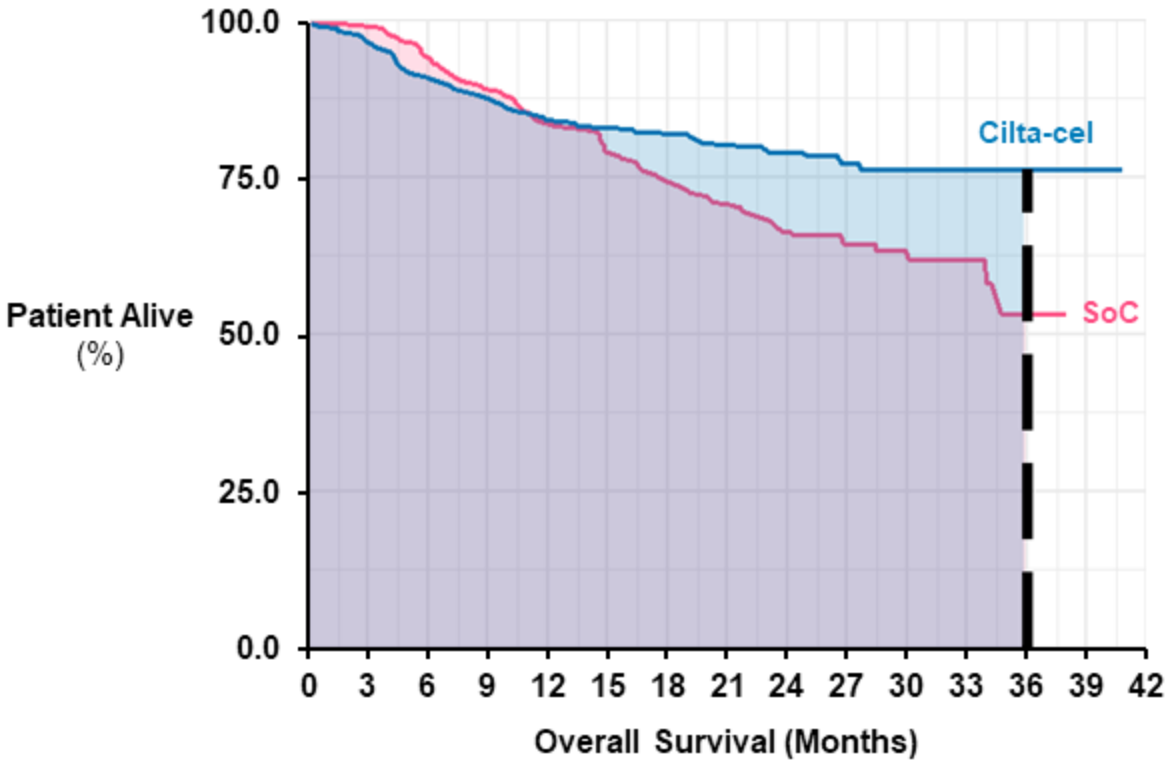
- Restricted Mean Survival Time (RMST)
  - Evaluated in the period from randomization to 22.4 months*
  - **Difference in RMST: 4.7 months (95% CI: 3.1, 6.1)**
  - **p < 0.0001**



* The smaller value of the longest PFS event time observed from each of the two arms

Post-hoc Sensitivity Analysis of OS: RMST

- Restricted Mean Survival Time (RMST)
  - Evaluated in the period from randomization to 36 months
  - **Difference in RMST:**
    2.3 months (95% CI: 0.1, 4.5)



December 2023 Cutoff

Summary of Subsequent Anti-Myeloma Therapies
as of Nov 2022

Subsequent Anti-Myeloma Therapy, N (%)	Cilta-cel (N = 208)	Standard of Care (N = 211)
Patients with 1 or more subsequent anti-myeloma therapies	43 **(21%)**	112 **(53%)**
Class of therapy		
Chemotherapy	33 **(16%)**	55 **(26%)**
Other therapies	28 **(14%)**	84 **(40%)**
Proteasome inhibitors	20 **(10%)**	62 **(29%)**
Monoclonal antibodies	12 **(6%)**	52 **(25%)**
Immunomodulatory agents	9 **(4%)**	19 **(9%)**
HDT+ASCT	3 **(1%)**	1 **(1%)**
Antibody drug conjugates	2 **(1%)**	16 **(8%)**
Cellular therapy		
Autologous BCMA CART therapy (cilta-cel)	20* **(10%)**	**0**
Autologous BCMA (investigational)	**0**	5 **(2%)**
Autologous BCMA CART therapy (ide-cel)	**0**	2 **(1%)**
Other cellular therapy	**0**	7 **(3%)**

*Cilta-cel administered as subsequent systemic therapy to patients randomized to cilta-cel arm with PD event during bridging therapy

Table 4: Reasons for Treatment and Study Discontinuation, ITT Population

Reasons for Discontinuation	Cilta-cel N=208 n (%)	Standard Therapy N=211 n (%)	Total N=419 n (%)
Treatment discontinuation	**32 (15)^**	**131 (63)**	**163 (39)**
Adverse event	0	3 (1.4)	3 (0.7)
Death	2 (1)	5 (2.4)	7 (1.7)
Progressive disease	30 (14)	117 (56)	147 (35)
Physician decision	0	1 (0.5)	1(0.2)
Withdrawal by patient	0	5 (2.4)	5 (1.2)
Study discontinuation	**39 (19)**	**51 (24)**	**90 (22)**
Death	39 (19)	47 (22)	86 (21)
Withdrawal by subject	0	4 (2)	4 (1)

Source: FDA analysis, data cutoff date November 1, 2022

^ Twenty subjects received cilta-cel after disease progression as subsequent therapy and 12 subjects did not receive cilta-cel.

Abbreviations: n (%), number of subjects with the specified characteristic; N, number of subjects in the specified group, or the total sample

Lower Pomalidomide and Bortezomib Dose Intensity May Have A Greater Risk for Early Progression

Pomalidomide	Q1 Dose Reduction* (N = 104)	Q2-Q4 (N = 311)
Early PFS	12 (11.5%)	16 (5.1%)

Bortezomib	Q1 Dose Reduction* (N = 13)	Q2-Q4 (N = 39)
Early PFS	7 (53.8%)	4 (10.3%)

* Dose reduction < 25% or lower of dose intensity

Primary and Key Secondary Endpoints: Subgroup Analysis in 1 Prior Line Population

1 Prior Line of Therapy Subgroup Nov 2022 CCO	Cilta-cel (N = 68)	Standard of Care (N = 68)	
Median PFS, months (95% CI)	**NE** (NE, NE)	**17** (11, NE)	**HR 0.45** (0.25, 0.80)
CR or better rate, %	**71** (58, 81)	**35** (24, 48)	**OR 4.4** (2.1, 9.1)
ORR, %	**90** (80, 96)	**79** (68, 88)	**OR 2.3** (0.9, 6.0)
MRD negativity rate, %	**63** (51, 75)	**19** (11, 31)	**OR 7.3** (3.3, 15.9)
Median Overall survival, months [Dec 23 CCO]	**NE** (NE, NE)	**NE** (NE, NE)	**HR 0.73** (0.36, 1.49)

Baseline Disease Characteristics in Patients in the Cilta-cel Arm with a PFS Event Prior to Cilta-cel Infusion (n = 32)

	Cilta-cel (N = 208)	Standard of Care (N = 211)	PFS Events Prior to Cilta-cel (n = 32)
ECOG PS			
0	55%	57%	11 (34%)
1/2	45%	43%	21 (66%)
ISS stage			
I	65%	63%	15 (47%)
II	29%	31%	15 (47%)
III	6%	7%	2 (6%)
Presence of soft tissue plasmacytomas	21%	17%	14 (44%)
Prior lines of therapy (LoT)			
1 prior LoT	33%	32%	8 (25%)
2 or 3 prior LoT	67%	68%	24 (75%)
Cytogenetic high risk	59%	63%	18 (56%)
Anti-CD-38-refractory	24%	22%	16 (50%)
PI-refractory	50%	46%	19 (59%)
Triple class refractory	14%	16%	10 (31%)