Abstract 1031
Phase 2 Registrational Study of Anitocabtagene Autoleucel for the Treatment of Patients with Relapsed and/or Refractory Multiple Myeloma: Preliminary Results From the iMMagine-1 Trial

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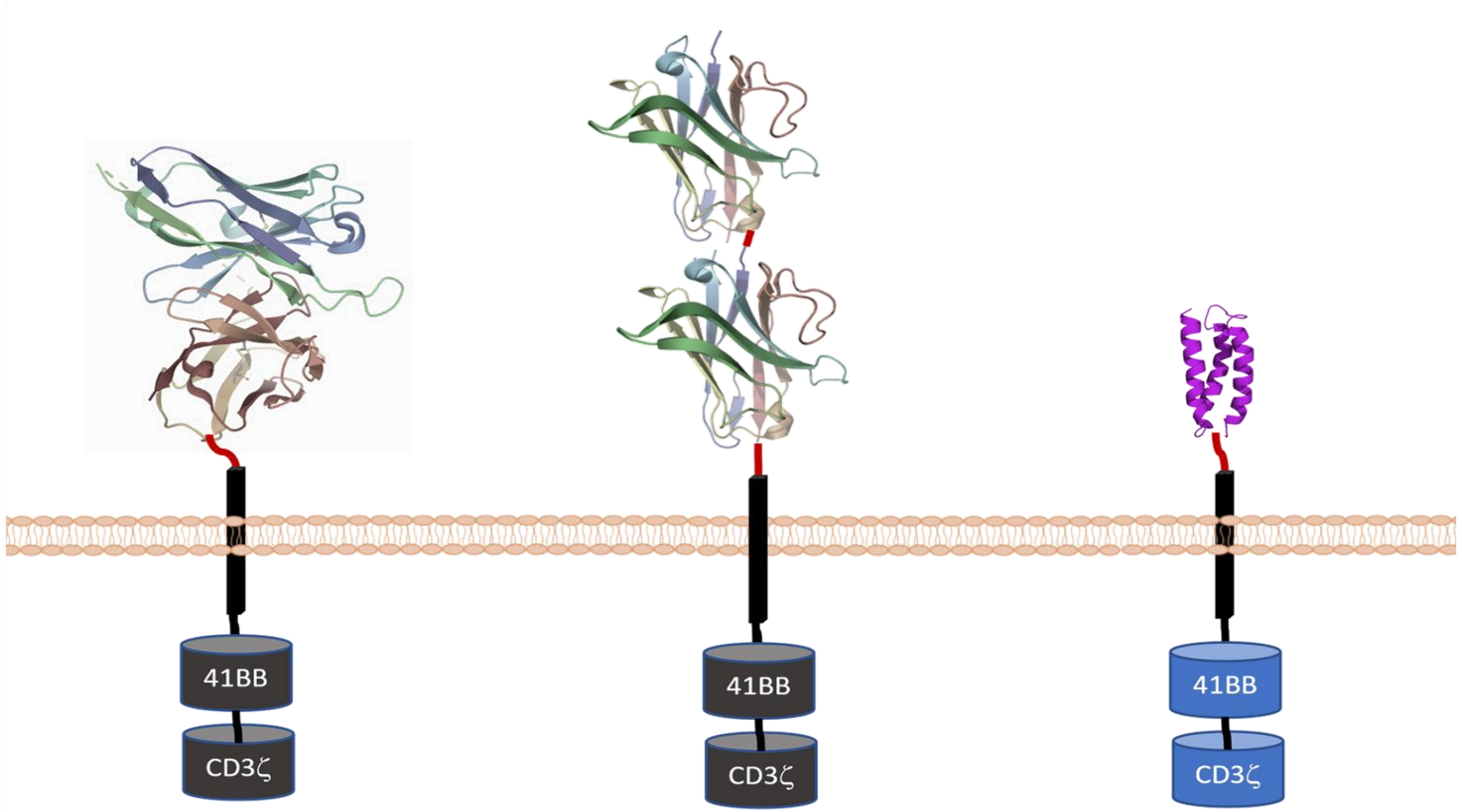
Anitocabtagene autoleucel (anito-cel/CART-ddBCMA)

Autologous BCMA-directed CAR T-cell therapy using a novel, D-Domain binder[1,2]



scFv
(~25 kDa)

Bivalent camelid VHH
(~30 kDa)

D-Domain
(~8 kDa)

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

Size

Small D-Domain construct facilitates high transduction efficiency and CAR positivity[2-4] resulting in a low total cell dose

Structure & Stability

D-Domain CARs are stable and lack tonic signaling[4,6] due to the rapid folding, lack of disulfide bonds, and hydrophobic core[5,6] of the D-Domain

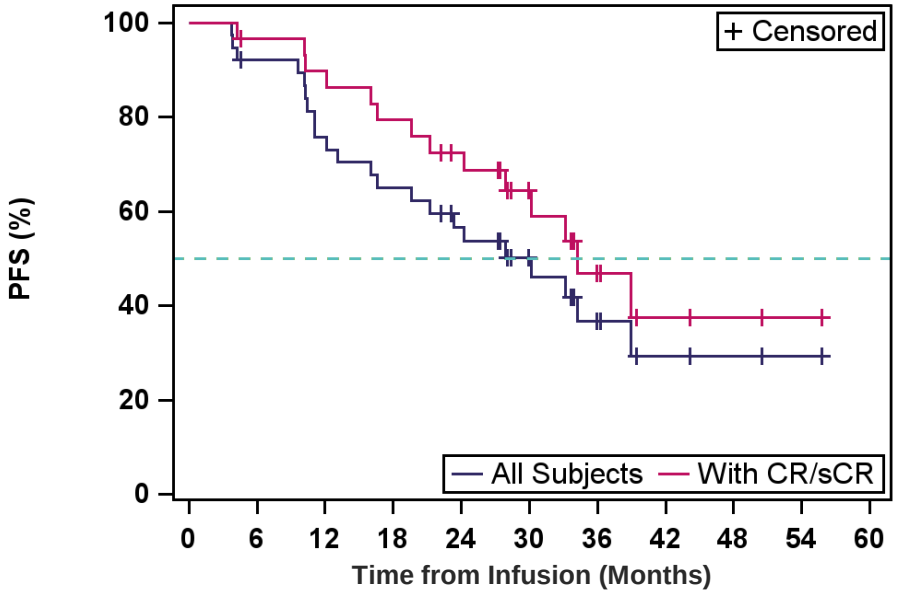
Binding

The D-Domain binder has a fast off-rate[4] and high CAR surface expression[4]. This combination may allow optimal tumor cell killing without prolonged inflammation

[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.

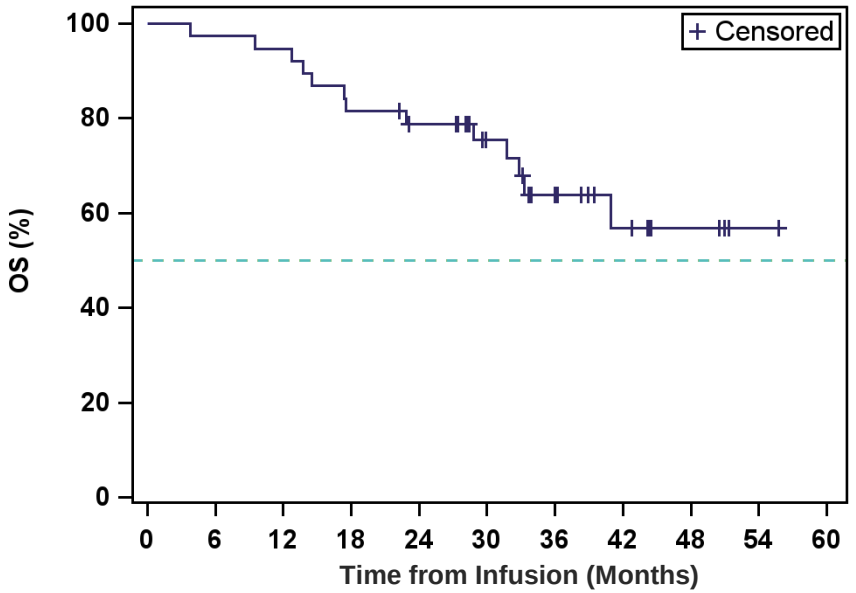
Background (ASH Poster 4825): Anito-cel Phase 1 demonstrated mPFS of 30.2 months in a 4L+ RRMM population, of whom 68% had high-risk features

Fig 1. Median PFS of 30.2 Months at 38.1 Months of Follow-up (N=38)



All Subjects	38	34	28	24	19	12	6	3	2	1	0
With CR/sCR	30	28	26	23	19	12	6	3	2	1	0

Fig 2. Median Overall Survival Not Reached (N=38)

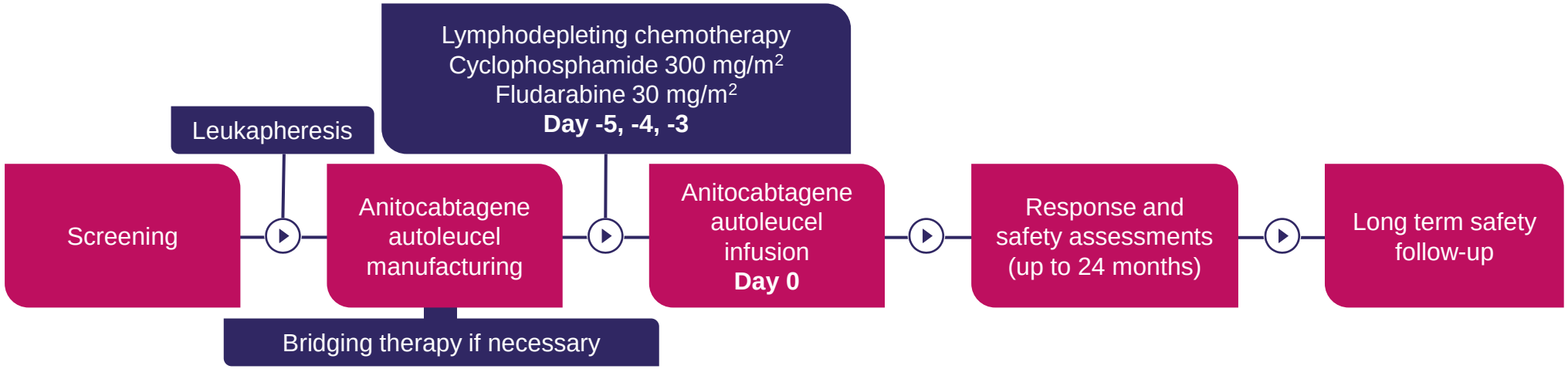


All Subjects	38	37	36	31	28	20	13	8	4	1	0

- **With a median follow-up of 38.1 months, anito-cel achieved rapid, high response rates with long-term durable remissions in a refractory, heavily pre-treated 4L+ RRMM population:**
  - sCR/CR achieved in 79% of patients
  - Median PFS of 30.2 months in all patients and 34.3 months in patients with sCR/CR
  - Median OS not reached
  - Similar efficacy and durable remissions were observed across high-risk subgroups
- **The safety profile is predictable and manageable with no delayed or non-ICANS neurotoxicities, including no Parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome**

Responses determined by IMWG Consensus Criteria
Bishop, et al. Blood 2024; ASH Annual Meeting, Poster #4825. Note: Data cut off: October 3, 2024

iMMagine-1: Phase 2 Study Design



Key Eligibility Criteria

- Prior IMiD, PI, and CD38-targeted therapy
- Received ≥3 prior lines of therapy
- Refractory to the last line of therapy
- ECOG PS of 0 or 1
- Evidence of measurable disease

Target Dose of 115 x 10^6 CAR+ T cells

Primary Endpoint:

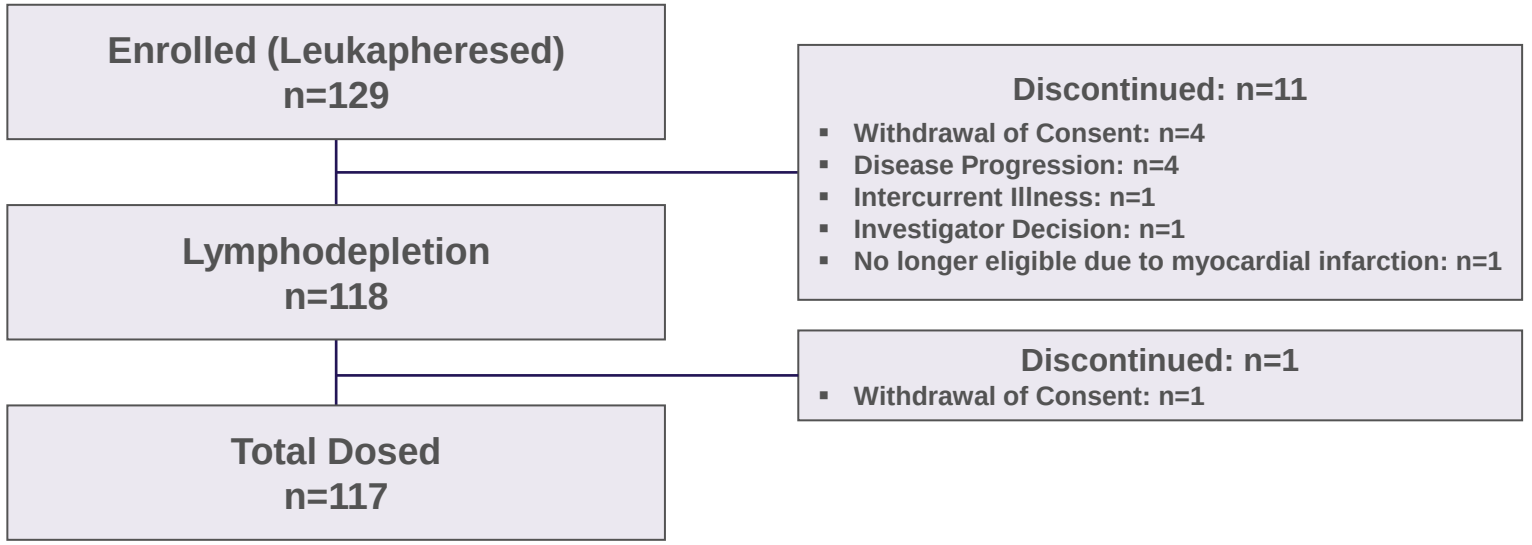
- ORR, per 2016 IMWG criteria

Key Secondary Endpoints:

- sCR/CR rate, per 2016 IMWG criteria
- ORR in patients limited to 3 prior LoT, per 2016 IMWG criteria

Primary and key secondary endpoints to be assessed per Independent Review Committee (IRC); Investigator assessment of response per IMWG also permitted per protocol.
CR, complete response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; LoT, line of therapy; ORR, overall response rate; PI, proteosome inhibitor; sCR, stringent complete response.

iMMagine-1: Overall Patient Disposition and Evaluable Populations



Safety Evaluable n=98

Subjects followed for ≥1 month by data cut-off of October 31, 2024 are evaluable for safety analysis

Efficacy Evaluable n=86

Subjects followed for ≥2 months by data cut-off of October 31, 2024 are evaluable for efficacy analysis

Anito-cel was successfully manufactured for 99% of patients enrolled

Total Patients Dosed per clinical database as of presentation date [12/09/2024]

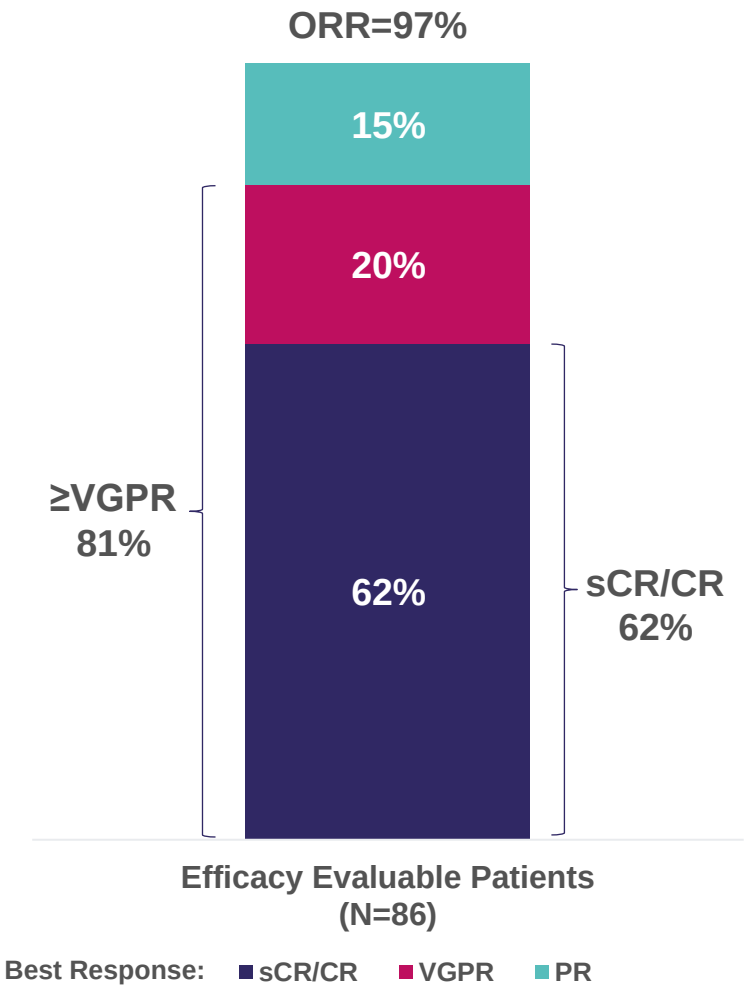
iMMagine-1: Patient and Disease Characteristics

Characteristics	Safety Evaluable (n=98)	Efficacy Evaluable (n=86)
Age (yrs), median (min - max)	65 (38 – 78)	65 (38 – 78)
Age ≥ 65	51 (52%)	47 (55%)
Age ≥ 70	30 (31%)	28 (33%)
Age ≥ 75	10 (10%)	10 (12%)
Gender (male / female)	55 (56%) / 43 (44%)	48 (56%) / 38 (44%)
Race		
White	79 (81%)	70 (81%)
Black / African American	9 (9%)	8 (9%)
Asian / Other	10 (10%)	8 (9%)
ECOG PS 0 / 1	45 (46%) / 53 (54%)	39 (45%) / 47 (55%)
Extramedullary disease[a]	16 (16%)	13 (15%)
High Risk Cytogenetics[b]	39 (40%)	33 (38%)
Refractory to last line of therapy	98 (100%)	86 (100%)
Triple refractory	85 (87%)	74 (86%)
Penta refractory	41 (42%)	37 (43%)
Prior Lines of Therapy, median (min - max)	4 (3 – 8)	4 (3 – 8)
3 Prior LoT	45 (46%)	37 (43%)
Time since diagnosis (yrs), median (min-max)	7.2 (1 – 23)	7.5 (1 – 23)
Prior ASCT	73 (75%)	64 (74%)
Bridging therapy	65 (66%)	61 (71%)
Outpatient administration	8 (8%)	5 (6%)

a) Presence of a non-bone based plasmacytoma; b) Defined as the presence of Del 17p, t(14;16), or t(4;14).
ASCT, autologous stem cell transplant; ECOG PS, Eastern Cooperative Oncology Group Performance Status; LoT, line of therapy

iMMagine-1: Overall Response Rate and MRD Negativity

Efficacy Evaluable Patients (N=86)



- At a median follow-up of 9.5 months, ORR was 97% and sCR/CR rate was 62%
- 93.1% (n=54/58) of evaluable patients were MRD negative at minimum of 10^{-5} sensitivity

	Evaluable Patients	Months (min - max)
Median time to first response	83	1.0 (0.9 - 7.3)
Median time to MRD negativity of ≤10^{-5}	54	1.0 (0.9 - 6.4)

Responses are investigator assessed per IMWG criteria, ORR defined as partial response or better; MRD evaluable patients had an identifiable malignant clone in the baseline bone marrow sample and had a post-treatment bone marrow sample sufficient to assess MRD negativity
CR, complete response; MRD, minimal residual disease; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

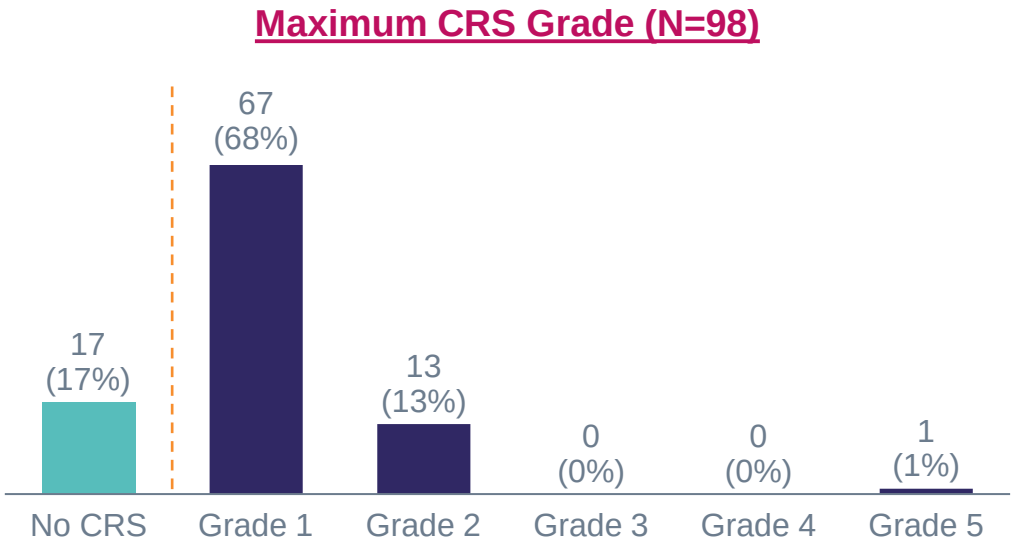
iMMagine-1: PFS and OS Rates Estimated by Kaplan-Meier

Efficacy Evaluable Patients (N=86)

	PFS Rate (%) (95% CI)	OS Rate (%) (95% CI)
6-Month	93.3% (84.4%, 97.2%)	96.5% (89.6%, 98.9%)
12-Month	78.5% (63.5%, 87.9%)	96.5% (89.6%, 98.9%)

Median follow-up of 9.5 months (range 2 to 23 months)
PFS, progression-free survival; OS, overall survival

iMMagine-1: Cytokine Release Syndrome



- 83% (81/98) of patients had CRS of any Grade; the median onset was 4 days
- 86% (84/98) of patients had CRS Grade 1 or less, including 17% (17/98) with no CRS
- % of patients with either no CRS or CRS that resolved by:
  - ≤7 days of anito-cel infusion: 63% (62/98)
  - ≤10 days of anito-cel infusion: 92% (90/98)
  - ≤14 days of anito-cel infusion: 98% (96/98)

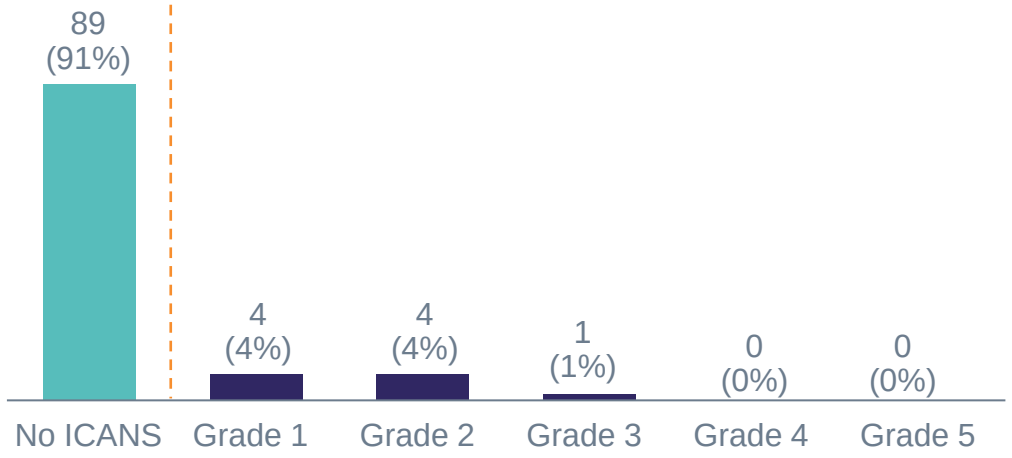
Cytokine Release Syndrome (CRS) Per ASTCT criteria	Safety Evaluable Patients N=98
Median onset (min-max)	4 days (1-17 days)
Median duration (min-max)	3 days (1-9 days)
Supportive Measures	
Tocilizumab	72% (71/98)
Dexamethasone	65% (64/98)
Anakinra	8% (8/98)
Siltuximab	4% (4/98)
Vasopressor used	1% (1/98)
Intubation/mechanical ventilation	1% (1/98)

- CRS management per protocol was in line with standard medical practice with no prophylactic administration of tocilizumab or dexamethasone
  - For CRS onset in the first 48 hours, tocilizumab and dexamethasone were protocol recommended
  - For CRS onset after the first 48 hours, if tocilizumab was administered at investigator discretion, dexamethasone was also recommended
- Grade 5 CRS occurred in a 76-year-old patient who had rapidly progressive disease between screening and baseline and did not receive bridging therapy

ASTCT, American Society for Transplantation and Cellular Therapy

iMMagine-1: Immune-effector Cell-associated Neurotoxicity Syndrome (ICANS)

Maximum ICANS Grade (N=98)



- 9% (9/98) of patients had ICANS of any grade; all cases resolved
- No delayed or non-ICANS neurotoxicities were observed, including no incidence of Parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome (n=98)
- Similarly, no delayed or non-ICANS neurotoxicities have been observed in the Phase 1 study[1] (n=38, median follow-up of 38.1 months with minimum follow-up of 25 months)

ICANS Per ASTCT criteria	Safety Evaluable Patients N=98
Median onset (min-max[a])	7 days (2 - 10[a] days)
Median duration (min-max[b])	4 days (1 - 10[b] days)
Supportive Measures	
Tocilizumab	3% (3/98)
Dexamethasone	6% (6/98)
Anakinra	1% (1/98)
Siltuximab	1% (1/98)

[a] With the exception of n=1 Grade 1 ICANS (confusion) on day 34 post infusion that rapidly resolved
[b] With the exception of n=1 max Grade 2 ICANS with 29-day duration to resolution

1. Bishop, et al. Blood 2024; ASH Annual Meeting, Poster #4825.
ASTCT, American Society for Transplantation and Cellular Therapy

iMMagine-1: Treatment-Emergent Adverse Events (Non-CRS/Non-ICANS)

	Any Grade AEs ≥20% after cell infusion (N=98)	Grade 3/4 AEs after cell infusion (N=98)
Hematologic		
Neutropenia	56 (57%)	53 (54%)
Anemia	24 (25%)	22 (22%)
Thrombocytopenia	20 (20%)	20 (20%)
Non-hematologic		
Fatigue	34 (35%)	2 (2%)
Hypophosphatemia	29 (30%)	2 (2%)
Nausea	28 (29%)	1 (1%)
Headache	27 (28%)	2 (2%)
Diarrhea	26 (27%)	1 (1%)
Hypogammaglobulinemia	23 (24%)	1 (1%)
Hypokalemia	21 (21%)	2 (2%)
Infections	44 (45%)	10 (10%)
Upper respiratory tract infection	9 (9%)	2 (2%)
Urinary tract infection	8 (8%)	2 (2%)
COVID-19	5 (5%)	1 (1%)

- The most common Grade 3 and higher treatment-emergent AEs (TEAEs) were cytopenias
- No replication competent lentivirus detected
- No secondary primary malignancies of T-cell origin or hematologic malignancies were reported
- Three deaths occurred due to TEAEs (related and unrelated to anito-cel)
  - Retroperitoneal hemorrhage* secondary to biopsy complication
  - CRS
  - Fungal infection

**At baseline prior to infusion, the patient developed plasma cell leukemia, which was an exclusion criteria. Evidence of Grade 4 hemophagocytic lymphohistiocytosis at time of death (only case to date).*
TEAE is defined as, 1) any AE with onset date on or after the first anito-cel infusion, until 90 days after the first anito-cel infusion regardless of causality assessment, or until start of subsequent anti-myeloma therapy, whichever is earlier; or 2) any AE occurring at any time assessed by the investigator as related to anito-cel

iMMagine-1: Conclusions

- **Anito-cel utilizes a novel, synthetic, compact and stable D-Domain binder**
  - D-Domain facilitates high transduction efficiency, CAR positivity, and CAR density on the T-cell surface and has a fast off-rate

- **Anito-cel demonstrated deep and durable efficacy at a median follow-up of 9.5 months**
  - ORR was 97% and sCR/CR rate was 62%, per IMWG criteria
  - 93.1% of MRD evaluable patients (n=54/58) were MRD negative at 10^{-5} or lower
  - Median PFS and OS not reached; 12-month PFS rate was 78.5% and OS rate was 96.5%

- **The anito-cel safety profile is predictable and manageable**
  - No delayed or non-ICANS neurotoxicities to date, including no Parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome reported across clinical trials
  - 86% of patients did not have CRS or had a max Grade 1 CRS
  - 91% of patients did not have ICANS

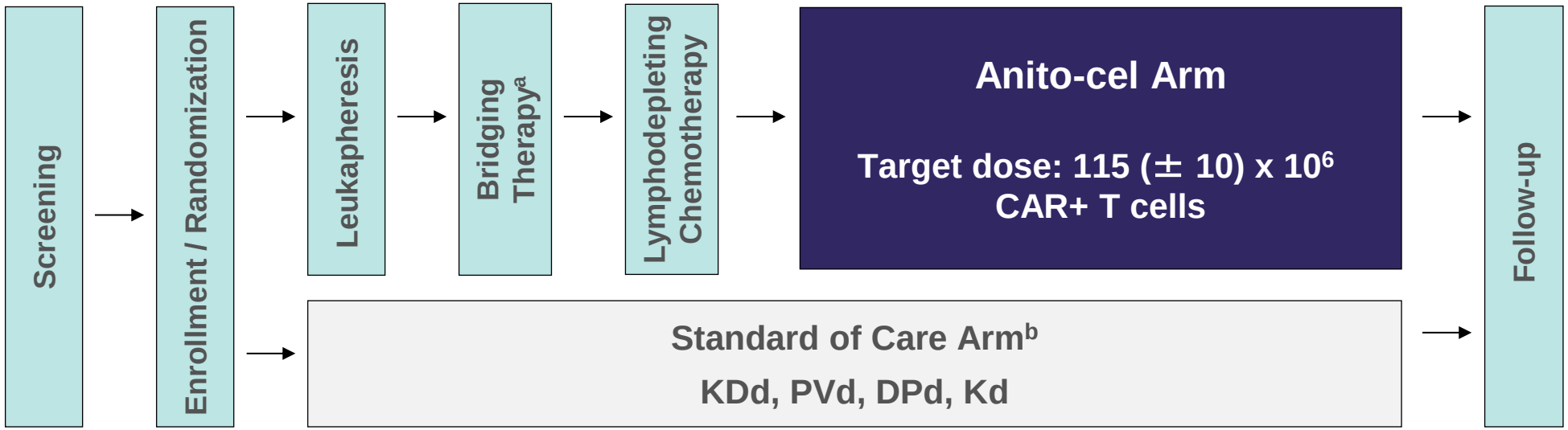
- **More than 150 patients dosed across the anito-cel programs for RRMM**

Anito-cel demonstrated deep, durable responses in 4L+ RRMM with a manageable safety profile, including no delayed or non-ICANS neurotoxicities

iMMagine-3 Design, Global Phase 3 Study – Now Enrolling

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

Anito-cel is being co-developed by Arcellx and Kite, and is being manufactured by Kite for iMMagine-3



Study Design

- 1:1 Randomization
- n = Approximately 450, ~130 sites globally

Study Endpoints

- Primary Endpoint: PFS
- Key Secondary Endpoints: CR rate, MRD, OS, safety

[a] *Optional Bridging therapy will be the SOC regimen selected prior to randomization*
[b] *Cycles will continue until unacceptable toxicity, progression as per IMWG criteria, or patient withdrawal of consent*

Acknowledgments

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- The staff, caregivers, research coordinators and investigators at each participating institution

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