Abstract S201
Phase 2 Registrational Study of Anitocabtagene Autoleucel for Relapsed and/or Refractory Multiple Myeloma (RRMM): Updated Results from iMMagine-1

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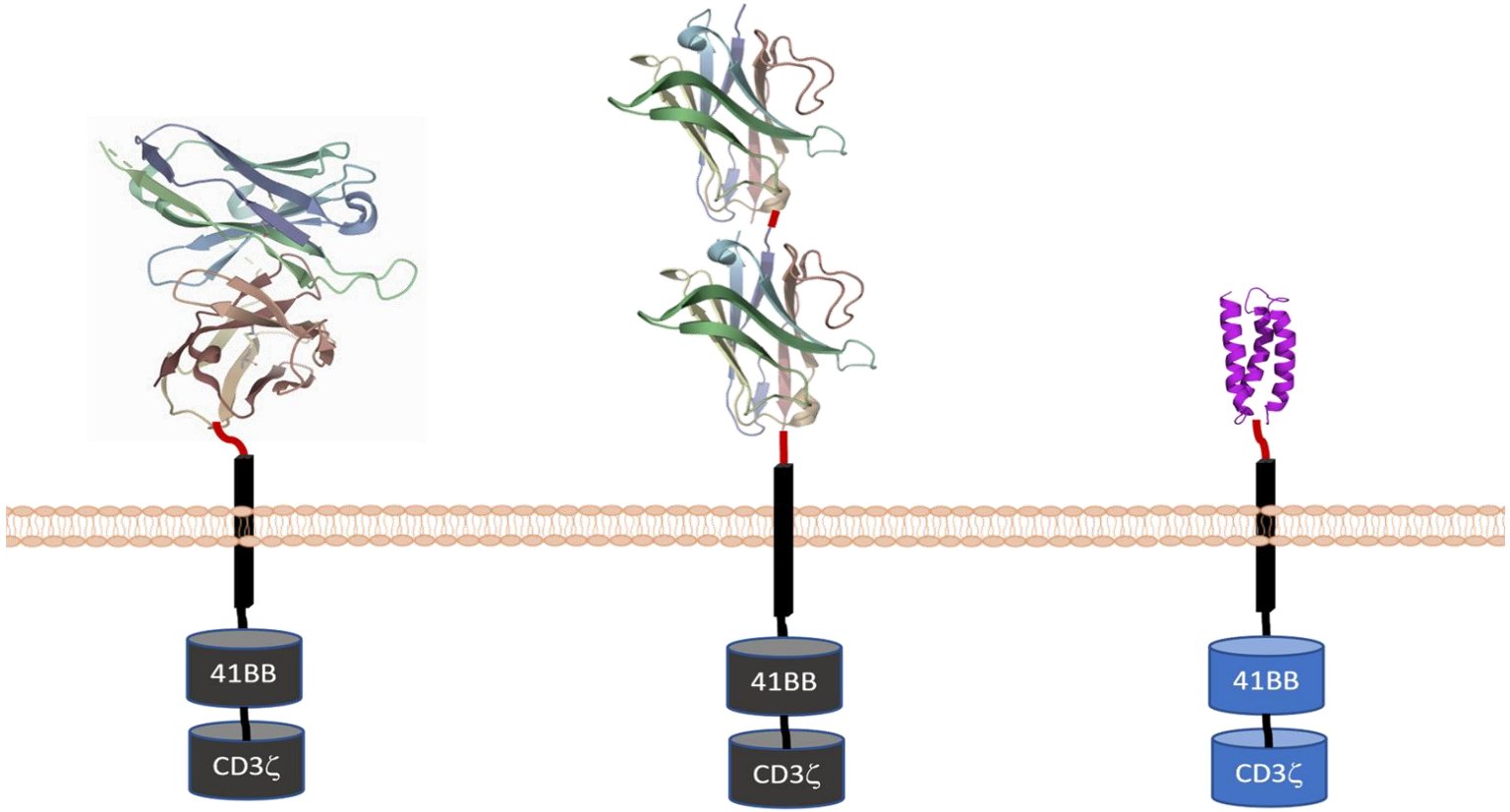
Anitocabtagene autoleucel (anito-cel/CART-ddBCMA)

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

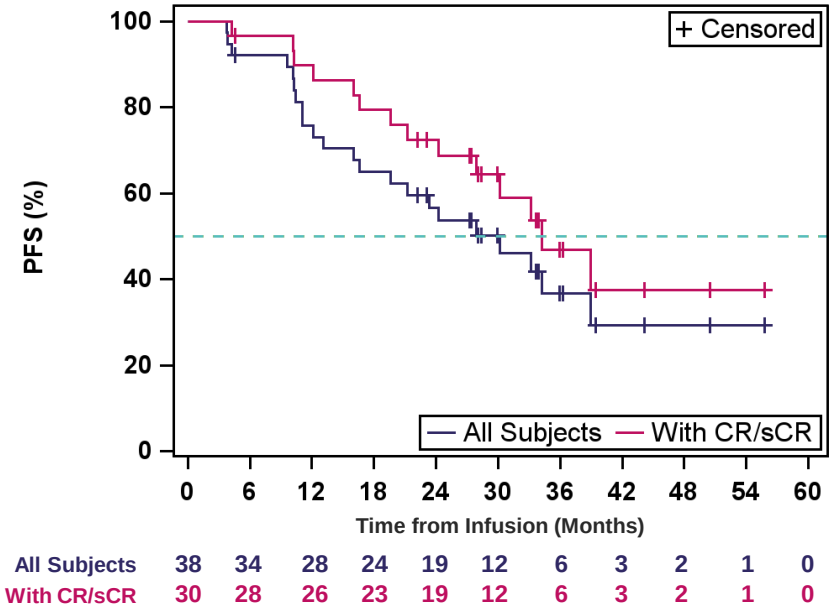
Binding

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

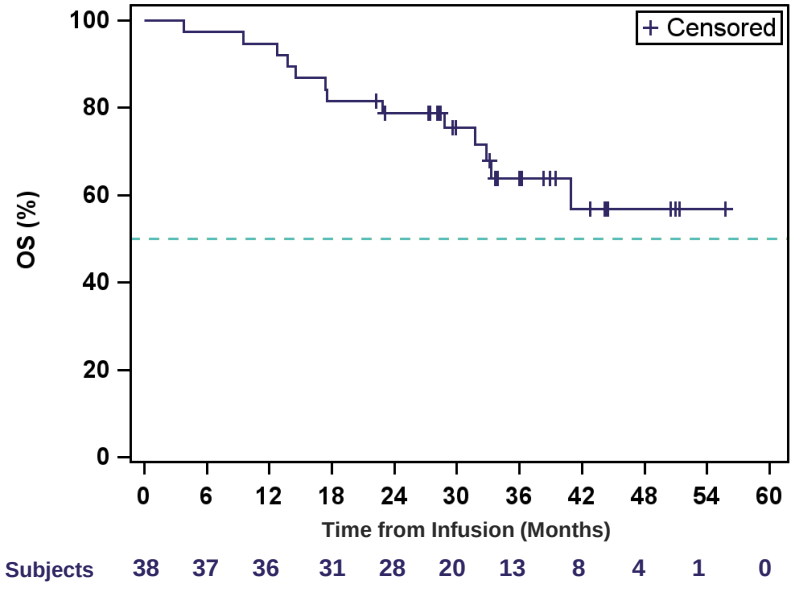
[1]Rotte, et al. Immuno-Oncology Insights 2022; 3(1), 13–24; [2]Frigault, et al. Blood Adv. 2023; 7(5):768-777; [3]Cante-Barrett, et al. BMC Res. Notes 2016; 9:13; [4]Buonato, et al. Mol. Cancer Ther. 2022; 21(7):1171-1183; [5]Zhu, et al. Proc. Nat. Acad. Sci. 2003; 100(26): 15486-15491; [6]Qin, et al. Mol. Ther. 2019; 27(7): 1262-1274.

Background: Anito-cel Phase 1 Demonstrated mPFS of 30.2 Months in a 4L+ RRMM Population

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



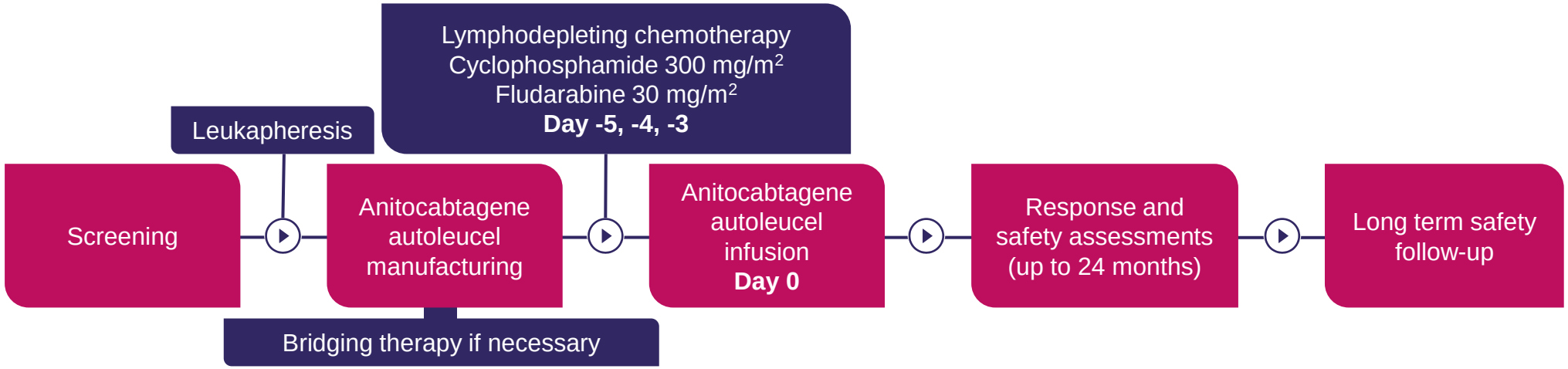
Median Overall Survival Not Reached (N=38)



- **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 (68% of patients had high-risk features)
- **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 MR, et al. Blood (2024) 144 (Supplement 1): 4825 as presented in poster #4825 at ASH 2024; 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

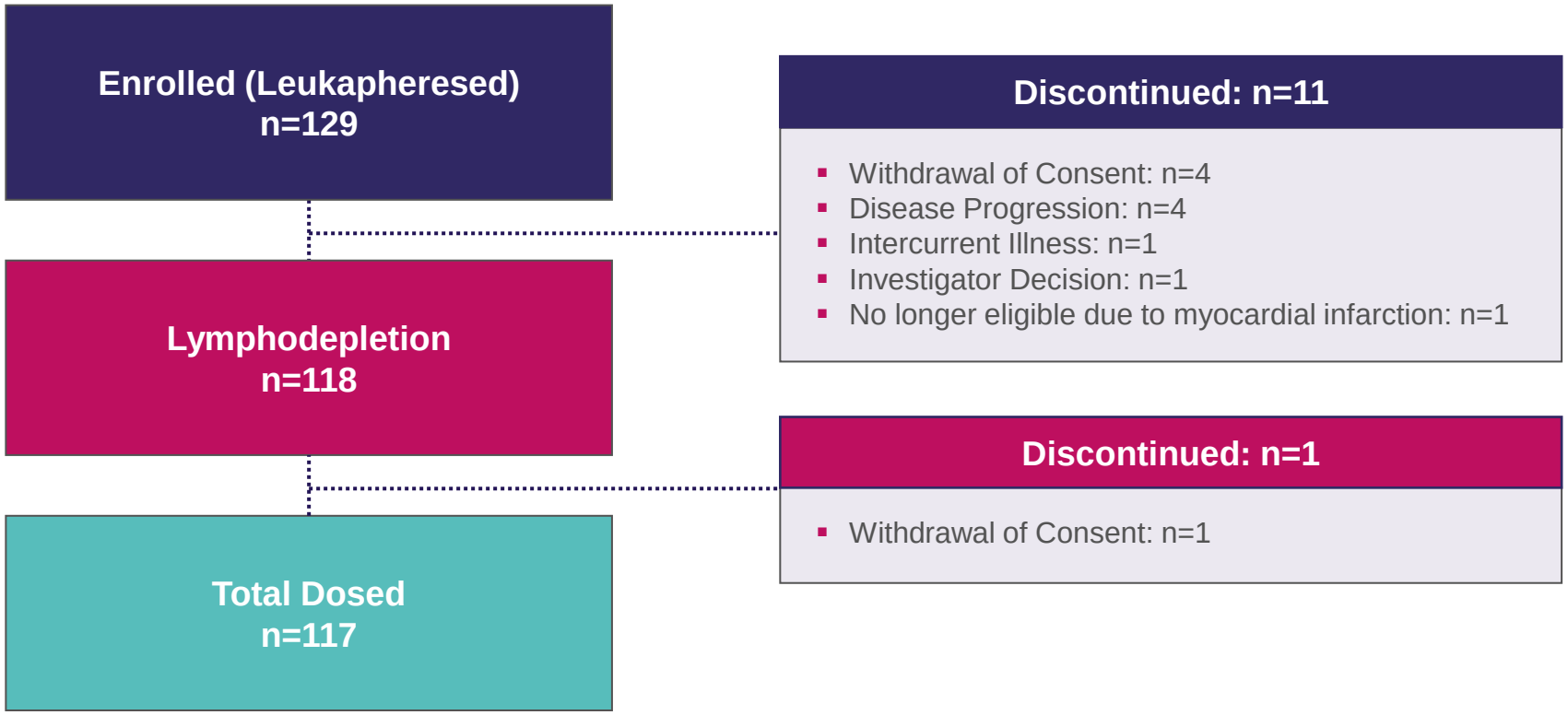
Key Secondary Endpoints:

- 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

Data cut-off: May 1, 2025; Median follow-up of 12.6 months (range: 5-29 months)



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

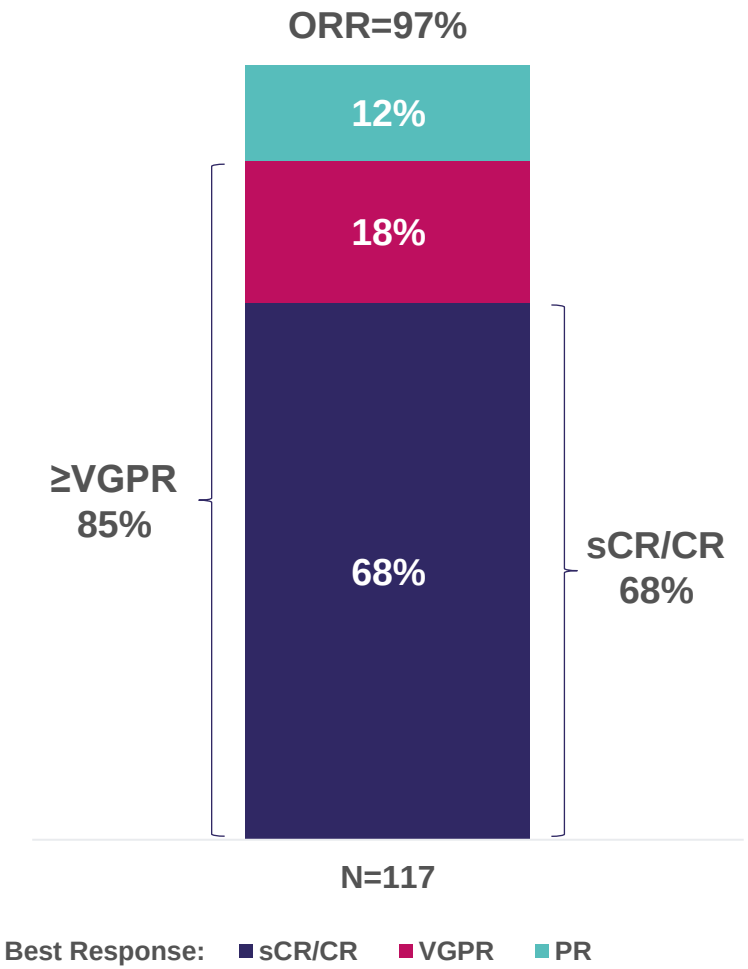
iMMagine-1: Patient and Disease Characteristics

Characteristics	N=117
Age (yrs), median (min - max)	64 (38 – 78)
Age ≥ 65	58 (50%)
Age ≥ 70	33 (28%)
Age ≥ 75	10 (9%)
Gender (male / female)	66 (56%) / 51 (44%)
Race	
White	89 (76%)
Black / African American	17 (15%)
Asian / Other	11 (9%)
ECOG PS 0 / 1	53 (45%) / 63 (54%)
Extramedullary disease[a]	18 (15%)
High risk cytogenetics[b]	44 (38%)
Refractory to last line of therapy	117 (100%)
Triple refractory	100 (86%)
Penta refractory	47 (40%)
Prior lines of therapy, median (min - max)	3 (3 – 8)
3 Prior LoT	60 (51%)
Time since diagnosis (yrs), median (min-max)	7.2 (1.0 – 23.1)
Prior ASCT	92 (79%)
Bridging therapy	88 (75%)
Outpatient administration	10 (9%)

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=117



- At a median follow-up of 12.6 months, ORR was 97% and sCR/CR rate was 68%
- 93% (n=70/75) of evaluable patients were MRD negative at minimum of 10^{-5} sensitivity

	Evaluable Patients	Months (min - max)
Median time to first response	114	1.0 (0.9 – 13.4)
Median time to MRD negativity of ≤10^{-5}	70	1.0 (0.9 – 6.4)

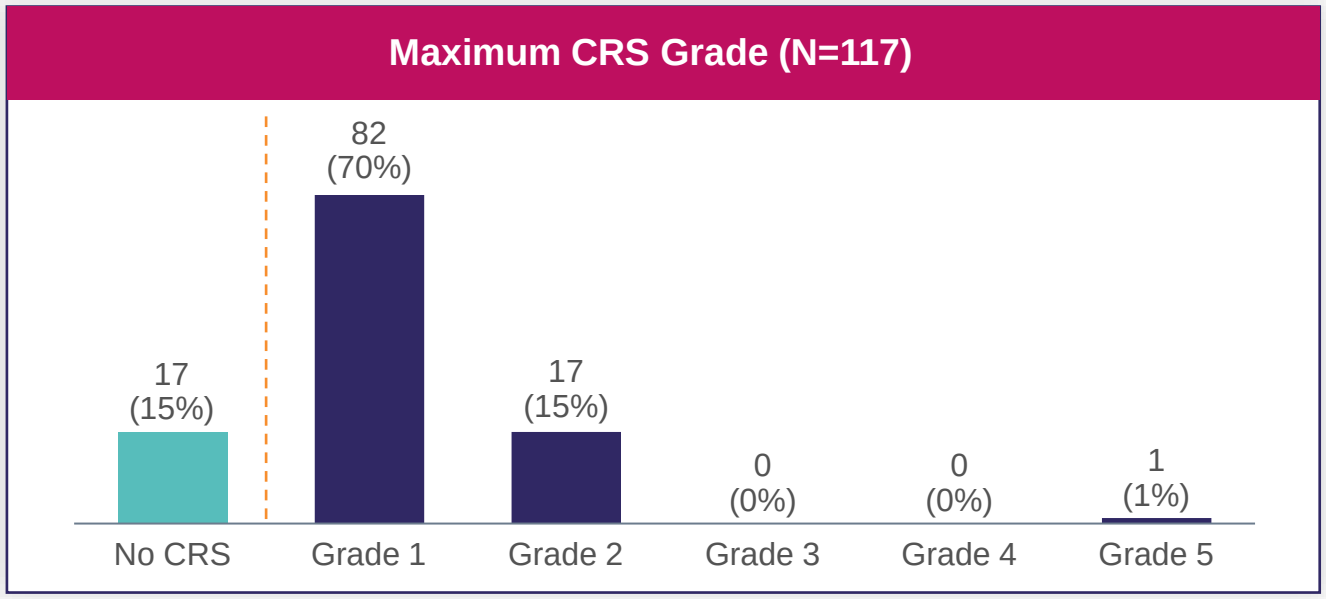
Responses are investigator assessed per IMWG criteria, ORR defined as partial response or better; MRD evaluable patients had an identifiable malignant clone in the baseline bone marrow sample and had a post-treatment bone marrow sample sufficient to assess MRD negativity
CR, complete response; MRD, minimal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

N=117	PFS Rate (%) (95% CI)	OS Rate (%) (95% CI)
6-Month	91.9% (85.0%, 95.7%)	96.6% (91.1%, 98.7%)
12-Month	79.3% (68.6%, 86.7%)	95.2% (88.7%, 98.0%)

Median follow-up of 12.6 months (range: 5 to 29 months)
PFS, progression-free survival; OS, overall survival

iMMagine-1: Cytokine Release Syndrome



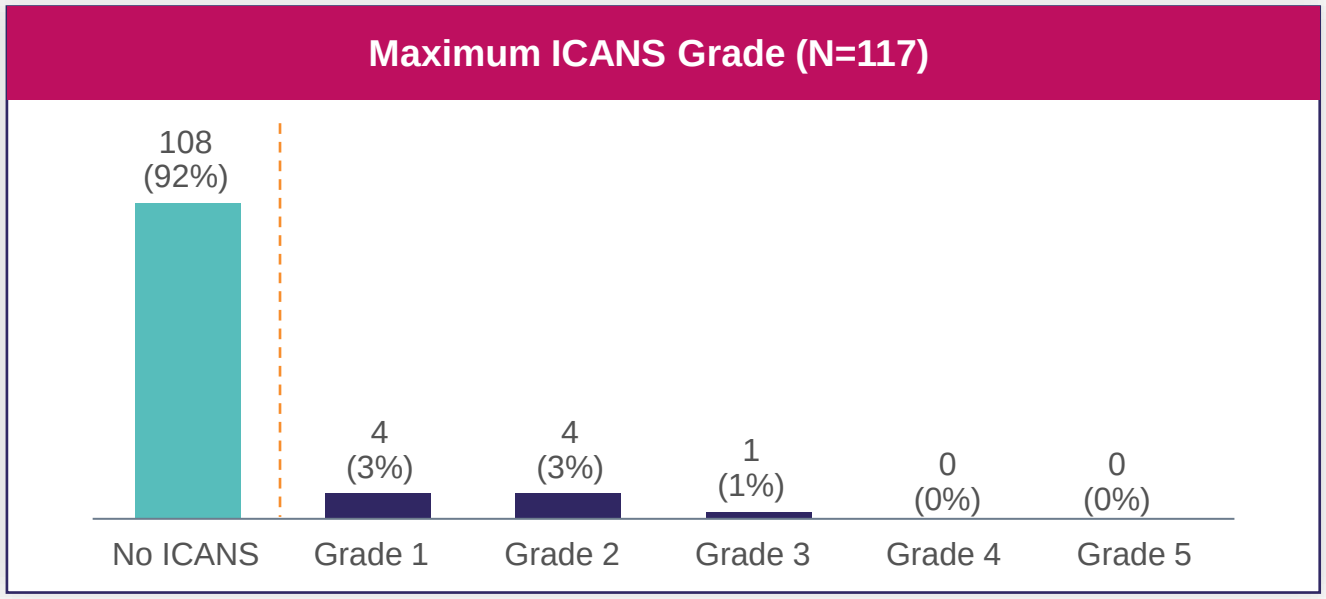
Cytokine Release Syndrome (CRS) Per ASTCT criteria	N=117
Median onset (min-max)	4 days (1-17 days)
Median duration (min-max)	2 days (1-9 days)
Supportive Measures	
Tocilizumab	77% (90/117)
Dexamethasone	73% (85/117)
Anakinra	11% (13/117)
Siltuximab	3% (4/117)
Vasopressor used	1% (1/117)
Intubation/mechanical ventilation	1% (1/117)

- 85% (99/117) of patients had CRS Grade 1 or less, including 15% (17/117) with no CRS; the median onset was 4 days
- % of patients with either no CRS or CRS that resolved by:
  - ≤7 days of anito-cel infusion: 80% (94/117)
  - ≤10 days of anito-cel infusion: 97% (114/117)
- 71% (83/117) of patients either received no dexamethasone or a single 10 mg dose of dexamethasone for CRS management

- 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 respond to bridging therapy

ASTCT, American Society for Transplantation and Cellular Therapy

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



ICANS Per ASTCT criteria	N=117
Median onset (min-max[a])	7 days (2-10[a] days)
Median duration (min-max[b])	4 days (1-12[b] days)
Supportive Measures	
Tocilizumab	3% (3/117)
Dexamethasone	5% (6/117)
Anakinra	1% (1/117)
Siltuximab	1% (1/117)

[a] With the exception of n=1 Grade 1 ICANS (confusion) on day 31 post infusion that rapidly resolved
[b] With the exception of n=1 max Grade 2 ICANS with 29-day duration to resolution

- 8% (9/117) 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=117; median follow-up of 12.6 months, range: 5-29 months)
- 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, range: 25-56 months)

1. Bishop MR, et al. Blood (2024) 144 (Supplement 1): 4825 as presented in poster #4825 at ASH 2024.
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=117)	Grade 3/4 AEs after cell infusion (N=117)
Hematologic		
Neutropenia	79 (68%)	77 (66%)
Anemia	32 (27%)	28 (24%)
Thrombocytopenia	28 (24%)	28 (24%)
Non-hematologic		
Fatigue	42 (36%)	3 (3%)
Hypogammaglobulinemia	40 (34%)	1 (1%)
Headache	35 (30%)	2 (2%)
Hypophosphatemia	34 (29%)	2 (2%)
Nausea	32 (27%)	1 (1%)
Diarrhea	32 (27%)	1 (1%)
Hypertension	23 (20%)	12 (10%)
Hypokalemia	23 (20%)	2 (2%)
Infections	61 (52%)	11 (9%)
Upper respiratory tract infection	15 (13%)	2 (2%)
Urinary tract infection	8 (7%)	2 (2%)
COVID-19	7 (6%)	1 (1%)

- The most common Grade 3 and higher treatment-emergent AEs (TEAEs) were cytopenias
- No cases of immune effector cell-associated enterocolitis have been reported
- 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
  - Cytokine Release Syndrome
  - 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 12.6 months**
  - ORR was 97% and sCR/CR rate was 68%, per IMWG criteria
  - 93% of MRD evaluable patients (n=70/75) were MRD negative at 10^{-5} or lower
  - Median PFS and OS were not reached; 12-month PFS rate was 79% and OS rate was 95%

- **The anito-cel safety profile is predictable and manageable**
  - No delayed or non-ICANS neurotoxicities, including no Parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome, and no immune effector cell-associated enterocolitis have been observed to date with anito-cel
  - 85% of patients did not have CRS or had a max Grade 1 CRS
  - 92% of patients did not have ICANS

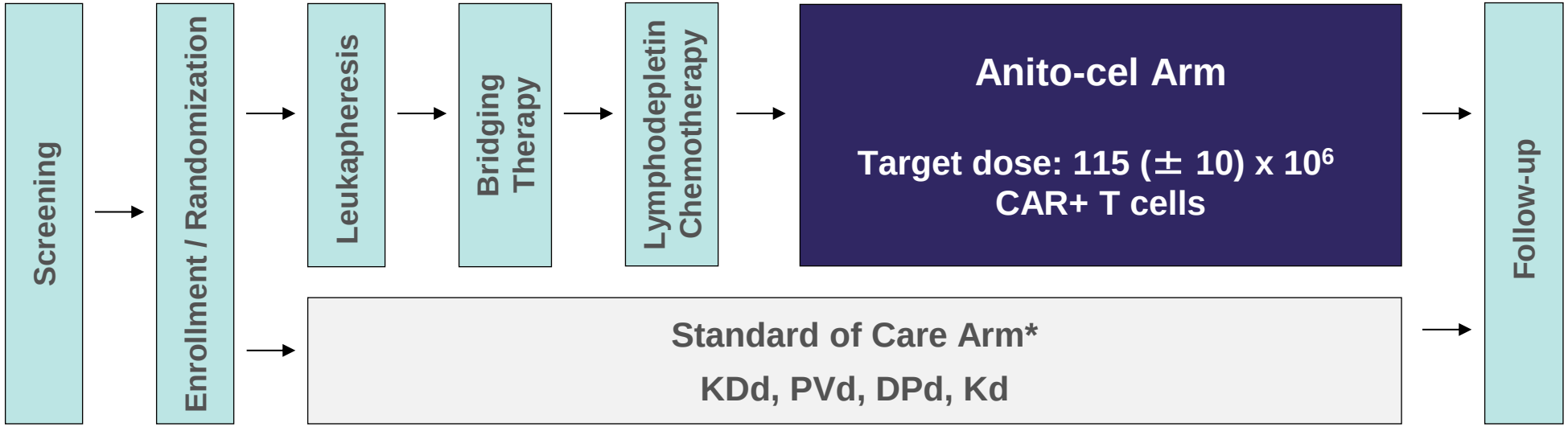
- **More than 150 patients dosed across the Phase 1 and Phase 2 anito-cel programs for RRMM**

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

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

**Cycles will continue until unacceptable toxicity, progression as per IMWG criteria, or patient withdrawal of consent*

Acknowledgments

We would like to thank:

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

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