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Phase 1 Study of Anitocabtagene Autoleucel for the Treatment of Patients with Relapsed and/or Refractory Multiple Myeloma (RRMM): Efficacy and Safety with 38.1-Month Median Follow-up

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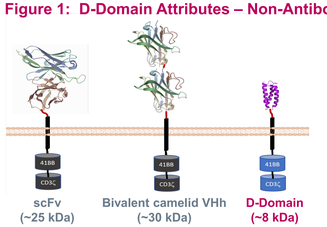
Introduction

- RRMM is characterized by progressively worse outcomes with each line of therapy[1], and novel therapies are needed to provide durable responses in later-line patients.
- While BCMA CAR T-cell therapies have demonstrated compelling clinical activity in patients with RRMM, outcomes continue to be limited particularly in patients with high-risk disease characteristics[2-4].
- Anitocabtagene autoleucel (anito-cel, previously CART-ddBCMA) is an autologous D-Domain BCMA-directed chimeric antigen receptor (CAR) T-cell therapy being studied in patients with RRMM.
- The BCMA-binding D-Domain is a small, synthetic 8 kDa protein comprised of 73 amino acids that fold into a stable triple alpha-helix bundle, resulting in several key attributes described in **Figure 1**[5,6].
- This report presents efficacy and safety results with a median follow-up of 38.1 months from the first-in-human Phase 1 study of anito-cel in patients with 4L+ RRMM.

Figure 1: D-Domain Attributes – Non-Antibody-Derived Synthetic Protein

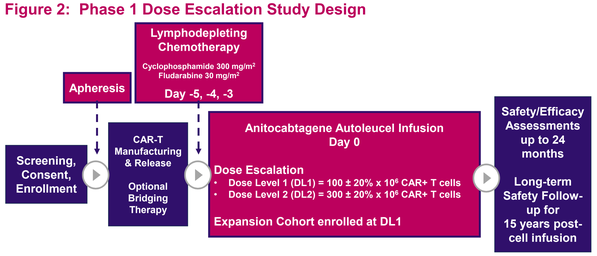


Size	Small D-Domain construct facilitates high transduction efficiency, CAR positivity, and CAR density on the T-cell surface[7,8]
Stability	Rapid D-Domain folding, lack of disulfide bonds, and a hydrophobic core enables D-Domain CAR stability[9,10]
Structure	Due to small size and compact structure, D-Domain CARs have a low risk of tonic signaling[10] and potentially more efficient multiple myeloma cell killing

Methods

- First-in-human Phase 1, multi-center, dose escalation trial in 4L+ RRMM
- Eligibility
  - At least 3 prior lines of therapy including a PI, IMiD, and anti-CD38 antibody; or triple-refractory disease following treatment with a PI, IMiD, and anti-CD38 antibody as part of the same or different regimens
  - Measurable disease per at least 1 of the criteria: serum M-protein ≥1.0 g/dL, urine M-protein ≥200 mg/24 hours; involved serum free light chain ≥100 mg/L with abnormal κ/λ ratio; >1 extramedullary lesion on imaging, including at least 1 lesion that is ≥1 cm and able to be followed by imaging assessments; or BMPCs ≥30%
  - ECOG PS of 0 or 1 and adequate organ function
- Primary Endpoints: Incidence of TEAEs, DLTs; establish the RP2D
- Select Secondary Endpoints: BOR and ORR by IMWG Consensus Criteria[11]
- Select Exploratory Endpoints: MRD negativity, DOR, PFS, OS
- Toxicity grading was performed per NCI CTCAE v 5.0, except for CRS and ICANS which were graded per ASTCT consensus criteria[12].
- Data cut-off: October 3, 2024

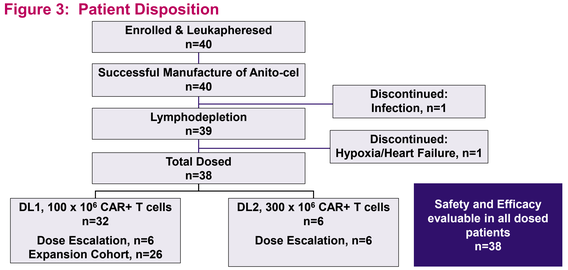
Figure 2: Phase 1 Dose Escalation Study Design



ASTCT, American Society for Transplantation and Cellular Therapy; BMPC, bone marrow plasma cell; BOR, best overall response; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status Scale; ICANS, immune effector cell-associated neurotoxicity; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MRD, minimal residual disease; NCI, National Cancer Institute; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteosome inhibitor; RP2D, recommended phase 2 dose; TEAE, treatment-emergent adverse event

Results

Figure 3: Patient Disposition



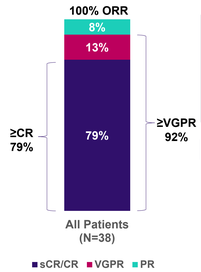
Median administered dose at DL1, 115 million cells (range, 112-120 million cells)

Table 1: Patient and Disease Characteristics

Characteristics	DL1: 100 x 10⁶ CAR+ T cells (n=32)	DL2: 300 x 10⁶ CAR+ T cells (n=6)	Total (n=38)
Age, median (min - max)	66 (44 - 76)	60 (52 - 65)	66 (44 - 76)
Age ≥ 65	19 (59%)	1 (17%)	20 (53%)
Gender, male / female	18 (56%) / 14 (44%)	5 (83%) / 1 (17%)	23 (61%) / 15 (39%)
Race			
White	28 (88%)	4 (67%)	32 (84%)
Black / African American	3 (9%)	1 (17%)	4 (11%)
Asian	1 (3%)	0 (0%)	1 (3%)
Other	0 (0%)	1 (17%)	1 (3%)
ECOG PS[a] 0 / 1	9 (28%) / 23 (72%)	3 (50%) / 3 (50%)	12 (32%) / 26 (68%)
High Risk Prognostic Feature[b]	20 (63%)	6 (100%)	26 (68%)
Prior Lines of Therapy, median (min - max)	5 (3 - 7)	4 (3 - 16)	4 (3 - 16)
Triple refractory	32 (100%)	6 (100%)	38 (100%)
Penta refractory	21 (66%)	5 (83%)	26 (68%)
Prior ASCT	25 (78%)	4 (67%)	29 (76%)
Time since diagnosis, median (min - max)	6.5 years (1.5 - 14.9 years)	6.9 years (1.7 - 11.0 years)	6.5 years (1.5 - 14.9 years)
Bridging therapy[c]	20 (63%)	6 (100%)	26 (68%)

a) Eastern Cooperative Oncology Group Performance Status Scale; b) Defined as a patient with EMD, ISS Stage III (B2M ≥ 5.5), High Risk Cytogenetics (Del17p, t(14;16), or t(4;14)), or BMPC ≥60%; c) Bridging agents were limited only to those previously received

Figure 4: Best Overall Response Rate and MRD Negativity



- 30 of 38 total patients (79%) achieved a CR/sCR
- 89% (n=25/28) of evaluable* patients were MRD negative at minimum of 10^{-5} sensitivity
- Responses were ongoing in 15 of 38 (39%) patients at a median follow-up of 38.1 months

	Months (min - max)
Median time to first response	1.0 (0.9 - 1.9)
Median time to best response	2.8 (0.9 - 19.4)
Median time to CR/sCR	2.8 (0.9 - 19.4)
Median time to MRD negativity of 10^{-5} or lower	1.0 (0.9 - 5.6)
Median duration of response (95% CI)	29.1 (15.8 - 38.0)

*Evaluable patients had identifiable malignant clone in the baseline bone marrow aspirate

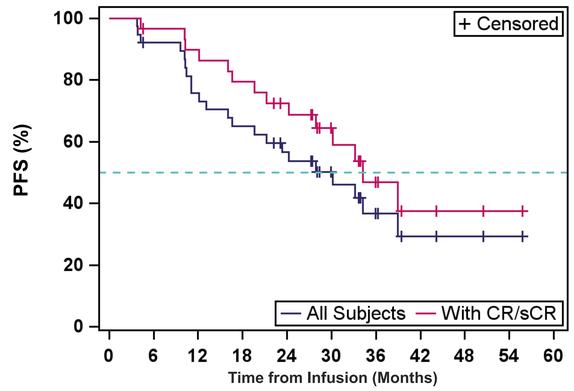
Table 2: Kaplan-Meier Estimated PFS Rates in All Patients & High-Risk Subgroups

	All Patients	High Risk Features*	Age ≥65 years
Patients n (%)	38 (100)	26 (68.4)	20 (52.6)
12-month PFS % (95% CI)	75.9 (58.7, 86.6)	72.2 (50.4, 85.7)	85.0 (60.4, 94.9)
24-month PFS % (95% CI)	56.6 (39.2, 70.8)	60.2 (38.7, 76.3)	65.0 (40.3, 81.5)
30-month PFS % (95% CI)	50.3 (33.0, 65.3)	60.2 (38.7, 76.3)	53.6 (29.5, 72.7)

The estimated median PFS has not been reached at 30 months for high-risk subgroups

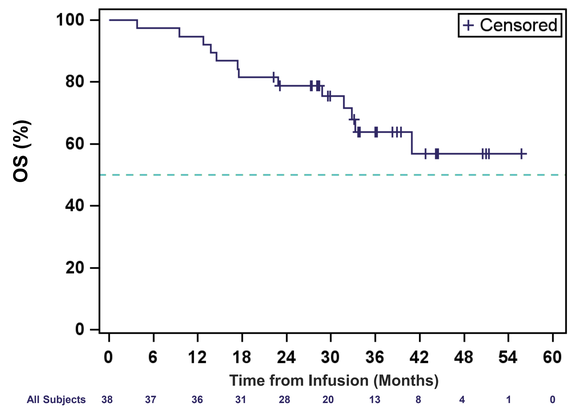
*High Risk Features defined as a patient with EMD, ISS Stage III (B2M ≥ 5.5), High Risk Cytogenetics (Del17p, t(14;16), or t(4;14)), or BMPC ≥60%

Figure 5: Median PFS for All Patients is 30.2 Months [95% CI: 16.6-39.0†]
Median PFS for CR/sCR Patients is 34.3 Months [95% CI: 24.2-NE]
Median Follow-up of 38.1 Months (Range: 25-56)



Estimated PFS Rate	All Patients (N=38) % (95% CI)	CR/sCR Patients (n=30) % (95% CI)
6-month PFS	92.1 (77.5, 97.4)	96.7 (78.6, 99.5)
12-month PFS	75.9 (58.7, 86.6)	89.8 (71.5, 96.6)
18-month PFS	65.0 (47.5, 78.0)	79.4 (59.8, 90.2)
24-month PFS	56.6 (39.2, 70.8)	72.5 (52.5, 85.2)
30-month PFS	50.3 (33.0, 65.3)	64.4 (43.7, 79.1)

Figure 6: Median OS for All Patients is Not Reached
Median Follow-up of 38.1 Months (Range: 25-56)



Estimated OS Rate	All Patients (N=38) % (95% CI)
6-month OS	97.4 (82.8, 99.6)
12-month OS	94.7 (80.6, 98.7)
18-month OS	81.6 (65.2, 90.8)
24-month OS	78.9 (62.1, 88.8)
30-month OS	75.4 (57.9, 86.5)

Safety

- No delayed or non-ICANS neurotoxicities have been observed at a median follow-up of 38.1 months
  - Including no incidence of Parkinsonism, no cranial nerve palsies, and no Guillain-Barré syndrome
- One patient had a Grade 5 event post study treatment (unrelated cardiac arrest due to non-study drug overdose)
- All secondary primary malignancies (SPMs) were required to be reported irrespective of relatedness or timing
  - No SPMs of T cell origin occurred
  - Hematologic SPMs of myelodysplastic syndrome (MDS) were reported in 3 patients as unrelated AEs by the investigator, and occurred in the setting of disease progression in patients heavily pre-treated with agents known to be associated with MDS

Table 3: CAR-T Associated AEs of CRS and ICANS per ASTCT Criteria (N=38)

CAR T-associated AEs Per ASTCT Criteria	DL1: 100 x 10⁶ CAR+ T cells (n=32)				DL2: 300 x 10⁶ CAR+ T cells (n=6)				Total (N=38)
CRS	**Gr1**	**Gr2**	**Gr3**	**Gr4**	**Gr1**	**Gr2**	**Gr3**	**Gr4**	**Any Gr**
Max grade, n (%)	15 (47%)	15 (47%)	0 (0%)	0 (0%)	3 (50%)	2 (33%)	1 (17%)	0 (0%)	36 (95%)
Median onset (min - max)	2 days (1 - 12 days)				2 days (1 - 2 days)				
Median duration* (min - max)	5 days (1 - 9 days)				5 days (3 - 9 days)				
ICANS	**Gr1**	**Gr2**	**Gr3**	**Gr4**	**Gr1**	**Gr2**	**Gr3**	**Gr4**	**Any Gr**
Max grade, n (%)	3 (9%)	2 (6%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	7 (18%)
Median onset (min - max)	4.5 days (3 - 6 days)				7 days				
Median duration (min - max)	3.5 days (1 - 9 days)				17 days				
Toxicity Management									
Tocilizumab	27 (84%)				5 (83%)				32 (84%)
Dexamethasone	20 (63%)				2 (33%)				22 (58%)

*Median duration numbers updated due to ongoing data review.

Table 4: Grade 3/4 AEs (non-CRS/ICANS) per CTCAE v5.0 ≥5% after cell infusion (N=38)

Hematologic	n (%)	Non-hematologic	n (%)
Neutropenia[a]	33 (86.8%)	Hypertension	3 (7.9%)
Anemia	21 (55.3%)	Pneumonia	3 (7.9%)
Thrombocytopenia[a]	17 (44.7%)	AST[b] increased	2 (5.3%)
Lymphopenia[a]	16 (42.1%)	Cardiac arrest	2 (5.3%)
Leukopenia[a]	8 (21.1%)	Cellulitis	2 (5.3%)
Febrile neutropenia	6 (15.8%)	Hypokalemia	2 (5.3%)
		Hyponatraemia	2 (5.3%)
		Hypophosphatemia	2 (5.3%)
		Pain in extremity	2 (5.3%)
		Sepsis[a]	2 (5.3%)
		Urinary tract infection	2 (5.3%)

a) Grouped category for each of the following: neutropenia, thrombocytopenia, lymphopenia, leukopenia, and sepsis;
b) Aspartate Aminotransferase Test

Conclusions

- Anito-cel utilizes a novel, synthetic, compact and stable D-Domain binder that facilitates high transduction efficiency, CAR positivity, and CAR density on the T-cell surface.
- 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 population of whom 68% had high-risk features:
  - ≥CR achieved in 79% of patients
  - Median PFS of 30.2 months in all patients and 34.3 months in patients with ≥CR
  - Median OS not reached
  - Similar efficacy and durable remissions were observed across high-risk subgroups
- 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 were observed across the Phase 1 and Phase 2 (iMMagine-1)[13] clinical trials.
- Anito-cel efficacy & safety compares favorably with available treatments for RRMM, including for RRMM bearing high-risk features.

Anito-cel is being co-developed with Kite's global cell therapy leadership

iMMagine-1 (NCT05396885) is the pivotal Phase 2 trial evaluating anito-cel in patients with RRMM and ≥3 prior LOT including a proteosome inhibitor, an IMiD, and an anti-CD38 monoclonal antibody

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

Acknowledgments

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

References

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†*Corrigendum*: The median PFS for all patients was reported at ASH 2024 as 30.2 months with a 95% confidence interval of 16.6-not estimable (NE). The correct data for median PFS for all patients is 30.2 months with a 95% confidence interval of 16.6-39.0.