Phase 1 Study of CART-ddBCMA for the Treatment of Patients with Relapsed and/or Refractory Multiple Myeloma: Results from at Least 1-year Follow-Up in All Patients

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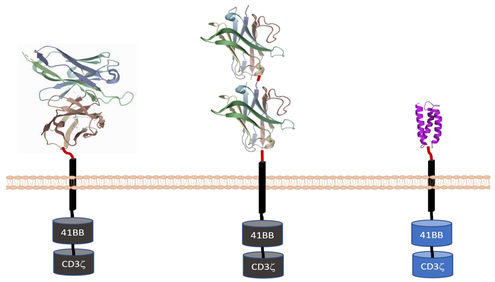
BACKGROUND

Anitocabtagene autoleucel (anito-cel/CART-ddBCMA)

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

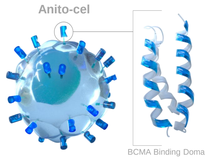
D-Domain Attributes:
Non-Antibody Derived Synthetic Protein[1,2]

Size	Stability	Structure
Small D-Domain construct facilitates high transduction efficiency, CAR positivity, and CAR density on the T-cell surface[2-4]	Rapid D-Domain folding, lack of disulfide bonds, and a hydrophobic core enables D-Domian CAR stability[5,6]	Due to small size and compact structure, D-Domain CARs have a low risk of tonic signaling[6] and potentially more efficient Multiple Myeloma cell killing



scFv (~25 kDa) | **Bivalent camelid VHh (~25 kDa)** | **D-Domain (~8 kDa)**

METHODS



Phase 1 first-in-human trial is in patients with relapsed and/or refractory myeloma

- Prior IMiD, PI, and CD38-targeted therapy
- Received ≥3 prior lines of therapies or triple refractory

Two Dose Levels evaluated, 6 patients in each dose escalation cohort

- DL1 = 100 ± 20% x 10^6 CAR+ cells
- DL2 = 300 ± 20% x 10^6 CAR+ cells

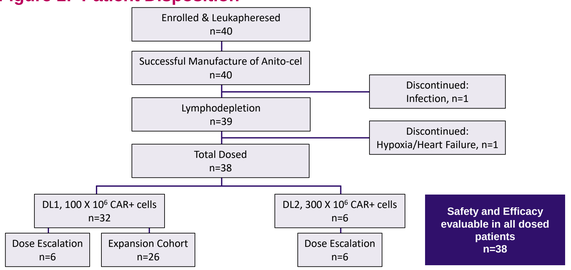
Data cut-off: October 15, 2023

Expansion cohort is enrolled at DL1

iMMagine-1: Phase 2 pivotal study (NCT05396885) is enrolling patients

RESULTS

Figure 1: Patient Disposition



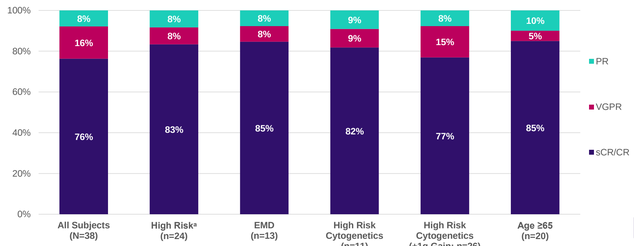
Median administered dose at DL1, 115 million cells (range, 112-120 million cells)

Table 1: Patient Demographics

Characteristics	Dose Level 1 100 million CAR-T (n=32)	Dose Level 2 300 million CAR-T (n=6)	Total (n=38)
Age, median (min - max)	66 (44 - 76)	60 (52 - 65)	66 (44 - 76)
Gender	18 Male (56%) 14 Female (44%)	5 Male (83%) 1 Female (17%)	23 Male (61%) 15 Female (39%)
ECOG PS[a] 0 1	 9/32 (28%) 23/32 (72%)	 3/6 (50%) 3/6 (50%)	 12/38 (32%) 26/38 (68%)
High Risk Prognostic Feature[b]	18/32 (56%)	6/6 (100%)	24/38 (63%)
BMPC ≥60%	6/32 (19%)	3/6 (50%)	9/38 (24%)
ISS Stage III (B2M ≥ 5.5)[b]	5/32 (16%)	2/6 (33%)	7/38 (18%)
Extra-medullary disease[c]	10/32 (31%)	3/6 (50%)	13/38 (34%)
High Risk Cytogenetics[d] Inclusive of 1q Gain	21/32 (66%)	5/6 (83%)	26/38 (64%)
High Risk Cytogenetics[d]	9/32 (28%)	2/6 (33%)	11/38 (29%)
Prior Lines of Therapy, Median (min - max)	5 (3 - 7)	4 (3 - 16)	4 (3 - 16)
Triple refractory	32/32 (100%)	6/6 (100%)	38/38 (100%)
Penta refractory	21/32 (66%)	5/6 (83%)	26/38 (68%)
Refractory to last line of therapy	28/32 (88%)	6/6 (100%)	34/38 (89%)
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	20/32 (63%)	6/6 (100%)	26/38(68%)
Previous ASCT	25/32 (78%)	4/6 (67%)	29/38(76%)

a) Eastern Cooperative Oncology Group Performance Status Scale; b) two additional patients in high risk resulting from ongoing data review; c) EMD is a form of Multiple Myeloma characterized by the presence of a non-bone based plasmacytoma; d) Defined as the presence of Del 17p, t(14;16), t(4;14).

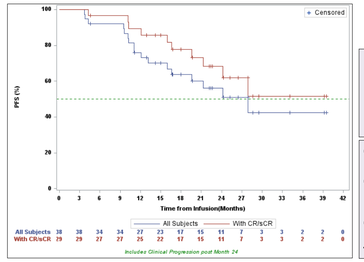
Figure 2: Best Overall Response



* High Risk defined as a patient with EMD, ISS Stage III (B2M ≥ 5.5), or BMPC ≥ 60%

Figure 3: All Patients, CR/sCR Patients

Median Follow-Up: All Patients 26.5-mo. [14-44]; CR/sCR Patients 26.5-mo. [15-44]



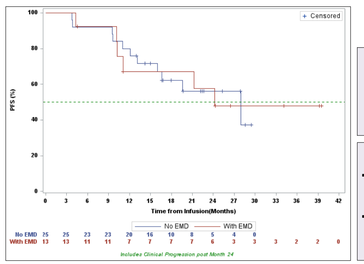
	Time (months)	PFS Estimate (%)	95% Confidence Interval (%)
All Patients (n = 38)	6	92.1	77.5, 97.4
	12	75.9	58.7, 86.6
	18	63.7	45.7, 77.2
	24	56.0	37.3, 71.1

- **Median PFS not reached for all patients (n=38)**
- **Median PFS not reached for CR/sCR patients (n=29, 76%)**
- **89% (n=25/28) of evaluable* patients MRD negative at minimum of 10^{-5} sensitivity**

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

Figure 4: Patients With or Without EMD

Median Follow-Up: EMD Patients ~33-mo. [14-44]; Non-EMD Patients ~25-mo. [15-40]



	Time (months)	PFS Estimate (%)	95% Confidence Interval (%)
With EMD (n = 13)	6	92.3	56.6, 98.9
	12	67.1	34.2, 86.2
	18	67.1	34.2, 86.2
	24	57.5	25.7, 79.9

- **Median PFS not reached for patients with EMD (n=13)**
- **Median PFS not reached for Non-EMD patients (n=25)**

Table 2: Kaplan-Meier Estimates

All Patients & High-Risk Subgroups

	Overall	High-Risk Features*	Extramedullary disease	High-Risk Cytogenetics	High-Risk Cytogenetics, Including 1q gain	≥ 65 years
Patients n (%)	38 (100%)	24 (63.2%)	13 (34.2%)	11 (28.9%)	26 (68.4%)	20 (52.6%)
6-month PFS % (95% CI)	92.1% (77.5%, 97.4%)	91.7% (70.6%, 97.8%)	92.3% (66.6%, 98.9%)	81.8% (44.7%, 95.1%)	92.3% (72.6%, 98.0%)	95.0% (69.5%, 99.3%)
12-month PFS % (95% CI)	75.9% (58.7%, 86.6%)	74.2% (51.3%, 87.5%)	67.1% (34.2%, 86.2%)	71.6% (35.0%, 89.9%)	76.3% (54.6%, 88.6%)	85.0% (60.4%, 94.9%)
18-month PFS % (95% CI)	63.7% (45.7%, 77.2%)	64.6% (41.3%, 80.6%)	67.1% (34.2%, 86.2%)	71.6% (35.0%, 89.9%)	67.0% (44.4%, 82.0%)	74.3% (48.7%, 88.4%)
24-month PFS % (95% CI)	56.0% (37.3%, 71.1%)	58.7% (35.1%, 76.3%)	57.5% (25.7%, 79.9%)	71.6% (35.0%, 89.9%)	62.2% (39.6%, 78.4%)	61.3% (34.9%, 79.7%)

In all risk subgroups, including High-Risk, the est. median PFS has not been reached at 24 months

* High-Risk defined as a patient with EMD, ISS Stage III (B2M ≥ 5.5), or BMPC ≥ 60%

Table 3 and Table 4: Safety

- No delayed neurotoxicities, no Guillain-Barré syndrome, no cranial nerve palsies, and no Parkinsonian-like syndromes in the entire population through the follow-up period
- One Grade 5 AE post study treatment (unrelated cardiac arrest due to non-study drug overdose)
- No change in safety profile as previously presented

Table 3

CAR-T-associated AEs Per ASTCT criteria	100 million (n=32)		300 million (n=6)	
Cytokine Release Syndrome (CRS)	Grade 1/2	Grade 3	Grade 1/2	Grade 3
	30 (94%)	0	5 (83%)	1 (17%)
Median onset (min-max)*	2 days (1-12 days)		2 days (1-2 days)	
Median duration (min-max)	6 days (1-10 days)		5 days (3-9 days)	
Neurotoxicity (ICANs)	Grade 1/2	Grade 3	Grade 1/2	Grade 3
	5 (16%)	1 (3%)	0	1 (17%)
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%)	
Dexamethasone	20 (63%)		2 (33%)	

Table 4

Grade 3/4 AEs (non-CRS/ICANS) ≥5% after cell infusion (n=38)	
Hematologic	
Neutrophil count decreased	31 (81.6%)
Anemia	22 (57.9%)
Thrombocytopenia	16 (42.1%)
Lymphocyte count decreased	15 (39.5%)
White blood cell count decreased	7 (18.4%)
Febrile Neutropenia	5 (13.2%)
Non-hematologic	
Hypertension	3 (7.9%)
AST[a] increased	2 (5.3%)
Cellulitis	2 (5.3%)
Hypokalemia	2 (5.3%)
Hyponatraemia	2 (5.3%)
Hypophosphatemia	2 (5.3%)
Lung Infection	2 (5.3%)
Pain in extremity	2 (5.3%)
Sepsis[b]	2 (5.3%)

Note: Median duration numbers updated due to ongoing data review; a) Aspartate Aminotransferase Test; b) Grouped category for sepsis

CONCLUSIONS

- **Anito-cel utilizes a novel, synthetic, compact and stable D-Domain binder**
  - D-Domain facilitates high CAR surface expression, low risk of tonic signaling
  - Recommended Phase 2 Dose selected as 115±10 million CAR+ T cells
- **CR/sCR rate 76%; 100% ORR per IMWG**
  - CR/sCR rate >77% in all sub-groups including high-risk (EMD, high-risk cytogenetics, age ≥65)
  - 89% of MRD evaluable patients (n=25/28) were MRD negative at 10^{-5} or lower
- **Median PFS, DOR, and OS not reached at 2 years of follow-up (median 26.5 months)**
  - Anito-cel continues to demonstrate deep and durable efficacy, including in high-risk patient sub-groups
- **At 2 years of follow-up (median 26.5 months), manageable safety profile**
  - No grade ≥3 CRS and 1 case of Grade 3 ICANS at RP2D. All events resolved without sequelae with routine management
  - No delayed neurotoxicity, no cranial nerve palsy, no Parkinsonian symptoms, no Guillain-Barré syndrome

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
See Martin *et al.*, Poster Number MM-382

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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.

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