Abstract # 8015

Phase 1 Study of CART-ddBCMA, a CAR-T therapy utilizing a novel synthetic binding domain for the treatment of subjects with relapsed and refractory Multiple Myeloma

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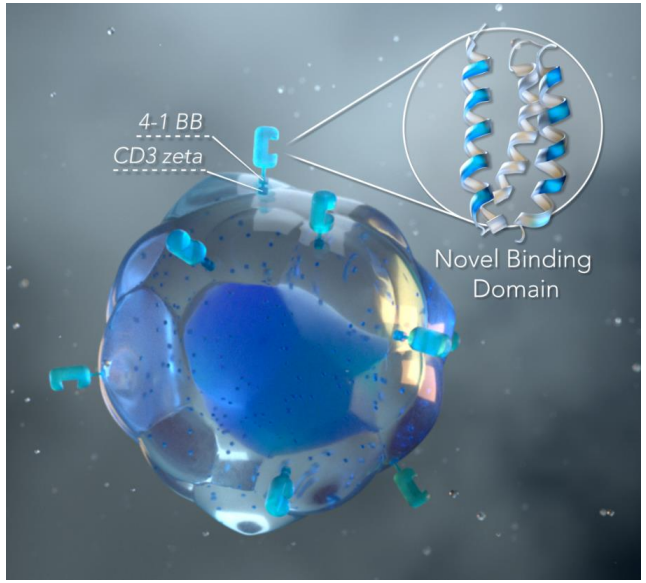
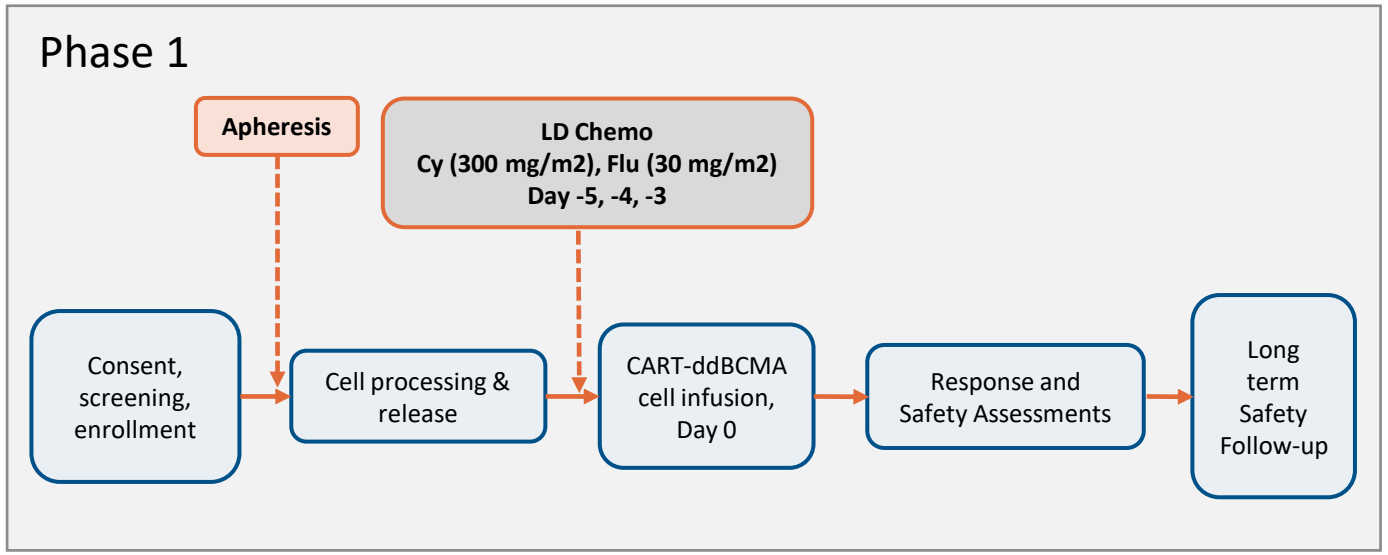
Background

- CART-ddBCMA is an autologous CAR-T containing a novel computationally designed synthetic protein[1] binding domain (non-scFv) engineered to reduce the risk of immunogenicity and is highly stable
- Phase 1 first-in-human trial is in progress, enrolling patients with relapsed and refractory myeloma
  - Prior IMiD, PI, and CD38-targeted therapy
  - Received ≥3 prior therapies or triple refractory





Patient Disposition (as of 14 Apr 2021)

16 subjects enrolled
- 13 subjects treated
  - 1 subject not yet evaluable
- 2 subjects pending treatment
- 1 subject d/c prior to cell infusion due to AE

Autologous drug products successfully and consistently manufactured for all subjects
- VCN median 2.33 (1.33–3.55)
- **CAR expression median 74.5% (61–87%)**

Subjects followed for <1 month are not yet evaluable and are not included in safety or efficacy analyses

Characteristics	Dose Level 1 100 million CAR-T (n=6)	Dose Level 2 300 million CAR-T (n=6)
Age, median (min-max)	73 (66-75)	60 (53-65)
Gender	3 Male 3 Female	5 Male 1 Female
BMPC >50%	3/6	4/6
Extra-medullary disease	4/6	3/6
High-risk cytogenetics per IMWG	5/5*	4/5*
Prior Lines of Therapy, median (min-max)	5 (5-7)	4 (3-16)
Prior HSCT	3/6	4/6
Penta-refractory	6/6	4/6
IgG myeloma IgA myeloma Light chain only	1 3 2	5 0 1

**1 subject not evaluable. BMPC = bone marrow plasma cells. HSCT = hematopoietic stem cell transplant*

[1]Qin, Haiying, et al. "Chimeric antigen receptors incorporating D domains targeting CD123 direct potent mono- and bi-specific antitumor activity of T cells." *Molecular Therapy* 27.7 (2019): 1262-1274

Adverse Events (as of 14 April 2021, N=12)

- 1 SAE related to CART-ddBCMA included ICANS
- No treatment-emergent Grade 3/4 infections

All Grade 3/4 AEs after cell infusion Regardless of Relatedness, (N=12)	
Hematologic	
Neutropenia	12
Febrile Neutropenia	4
Lymphocytopenia	12
Decreased hemoglobin	9
Thrombocytopenia	6
Decreased WBC	5
Coagulopathy	1
Non-hematologic	
Abdominal pain	1
Muscle hematoma	1
Hypertension	4
Hypotension	1
Electrolyte imbalance	4
Hyperglycemia	1

CAR-T-associated AEs Per ASTCT criteria	100 million (N=6)		300 million (N=6)	
Cytokine Release Syndrome (CRS)	**Grade 1/2**	**Grade 3**	**Grade 1/2**	**Grade 3**
	6	**0**	**5**	**1**
Median onset (min-max)	2.5 days (0-4 days)		< 24 hours (0-1 day)	
Median duration (min-max)	5 days (2-7 days)		3 days (1-9 days)	
Neurotoxicity (ICANs)	**Grade 1/2**	**Grade 3**	**Grade 1/2**	**Grade 3**
	1	**0**	**0**	**1**
Onset	2 days		6 days	
Duration	2 days		14 days	
Toxicity Management				
Tocilizumab	4		5	
Dexamethasone	3		2	
Anakinra	0		1	

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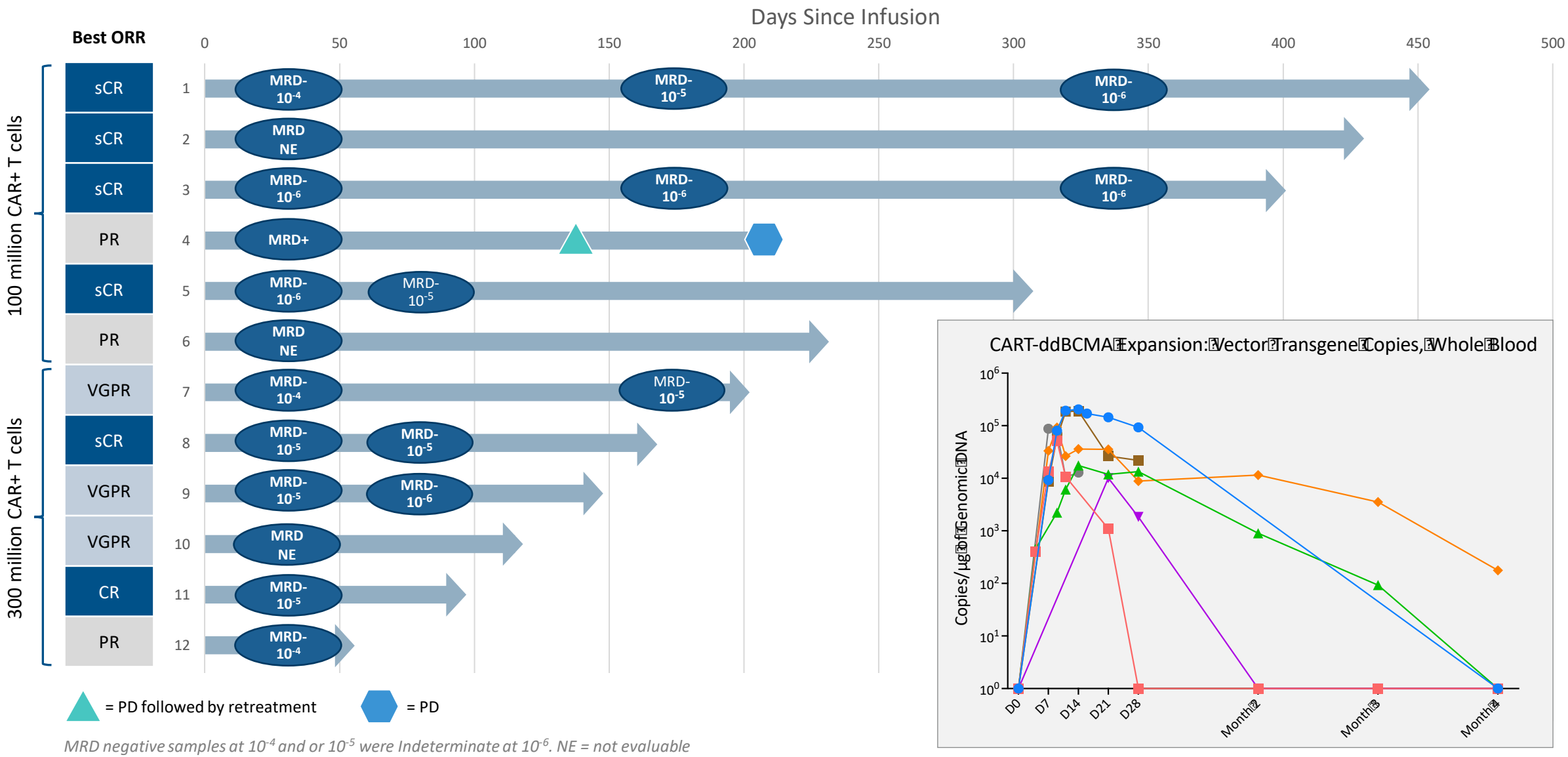
Days since CART-ddBCMA infusion (as of 14 Apr 21)

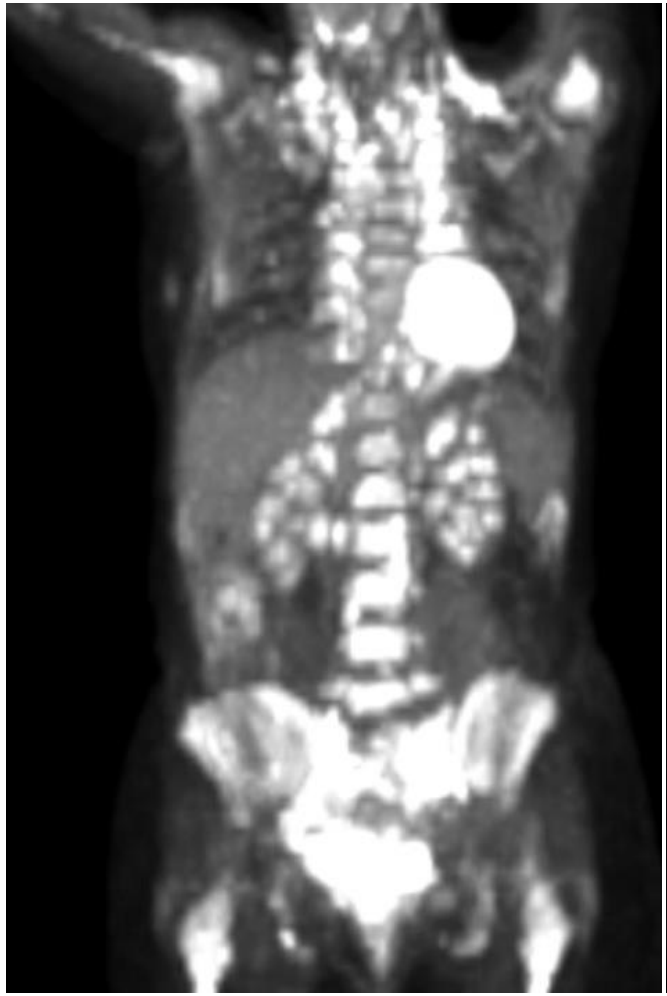
median follow-up = 197 days [min-max 29-449]



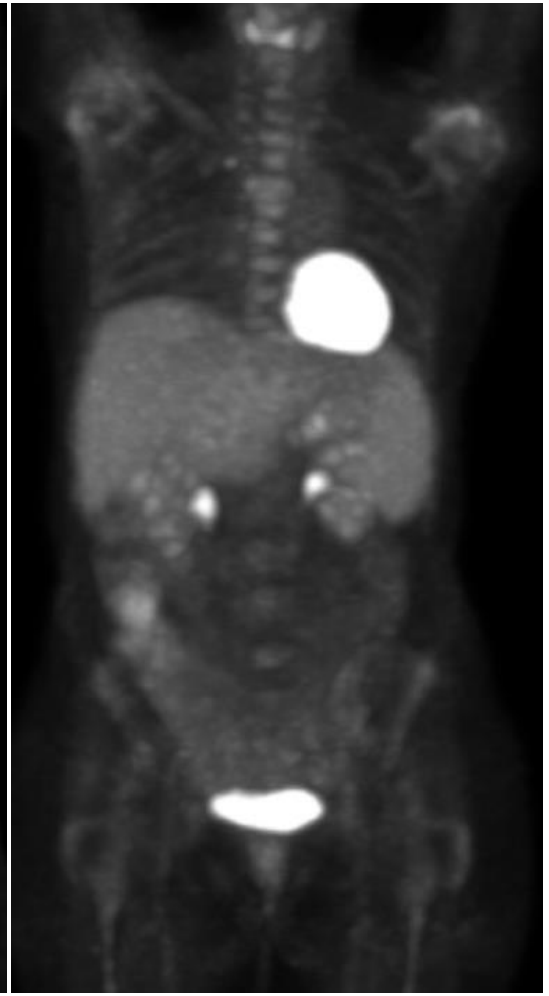
MRD negative samples at 10^{-4} and or 10^{-5} were Indeterminate at 10^{-6}. NE = not evaluable

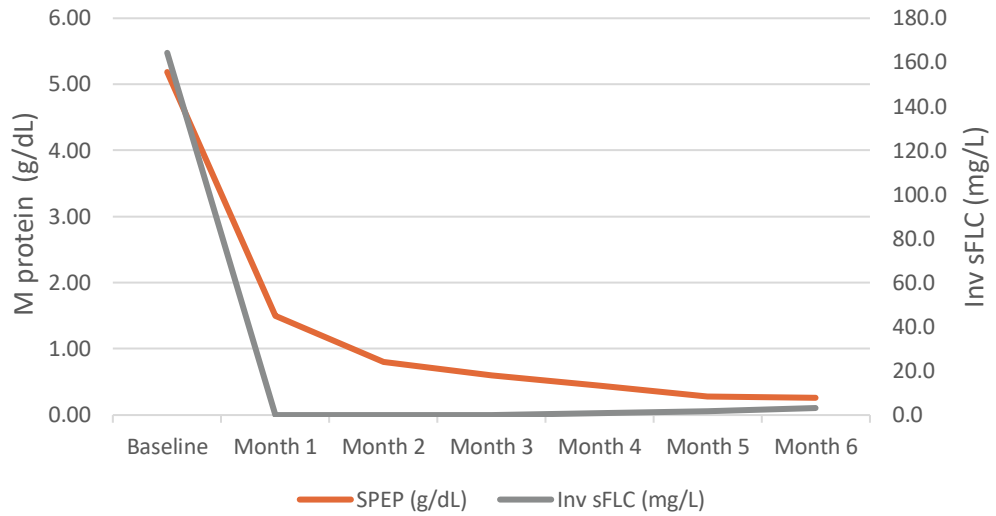
Subject #7: CART-ddBCMA induced response despite progression on prior BCMA-targeted therapy

Baseline



Month 1



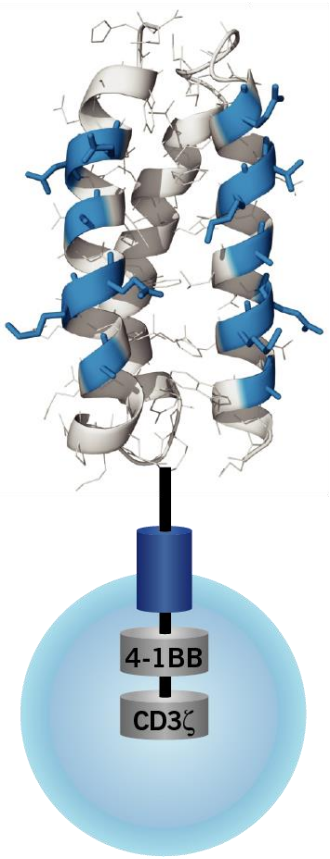


Bulky extra-medullary disease, bone marrow disease (50%) at baseline with high-risk cytogenetics, penta-refractory disease and prior failed therapy with BCMA-ADC

⇒ PET-CT negative by Month 1
⇒ Bone marrow negative by Month 1
⇒ MRD-negative 10^{-4} at Month 1
⇒ Remains MRD-negative 10^{-5} at Month 6

Conclusions

CART-ddBCMA



- **CART-ddBCMA utilizes a novel, non-scFv binding domain, that is highly stable and engineered to reduce immunogenicity**
  - 2 dose levels studied (100 million and 300 million CAR+ T cells); MTD not reached
- **Toxicities including CRS and ICANS have been manageable at both dose levels**
  - No off-target toxicities observed to date
- **100% ORR per IMWG across both dose levels; deep and durable responses observed in patients with poor prognostic factors**
  - 12/12 ORR: 6 CR/sCR, 3 VGPR, 3 PR
  - 11/12 responses are ongoing; responses continue to deepen
- **Ongoing Phase 1 expansion at 100 million CAR+ T cells given favorable safety profile and 100% ORR**
- **Pivotal phase 2 trial planned**

Thank you to the patients and their families, the healthcare professionals who cared for the patients, and the study staff who supported this clinical trial