



American Society of Hematology

Helping hematologists conquer blood diseases worldwide

First-in-Human Study of the Allogeneic Anti-BCMA ALLO-715 CAR T cell Therapy and the Anti-CD52 Mab ALLO-647 in Relapsed/Refractory Multiple Myeloma (UNIVERSAL Study)

Sham Mailankody¹, Jeffrey Matous², Michaela Liedtke³, Surbhi Sidana⁴, Shahbaz Malik⁵, Rajneesh Nath⁶,
Olalekan O. Oluwole⁷, Erin E. Karski⁸, Wade Lovelace⁸, Xiangdong Zhou⁸, Srinand Nandakumar⁸,
Arun Balakumaran⁸, Parameswaran Hari⁹

¹ Myeloma Service and Cellular Therapeutics Center, Memorial Sloan Kettering Cancer Center, NY, NY; ² Colorado Blood Cancer Institute/Sarah Cannon Research Institute, Denver, CO;

³ Division of Hematology, Stanford University School of Medicine, Stanford, CA; ⁴ Division of Blood and Marrow Transplantation and Center for Cell Therapy, Stanford Cancer Institute, Stanford, CA;

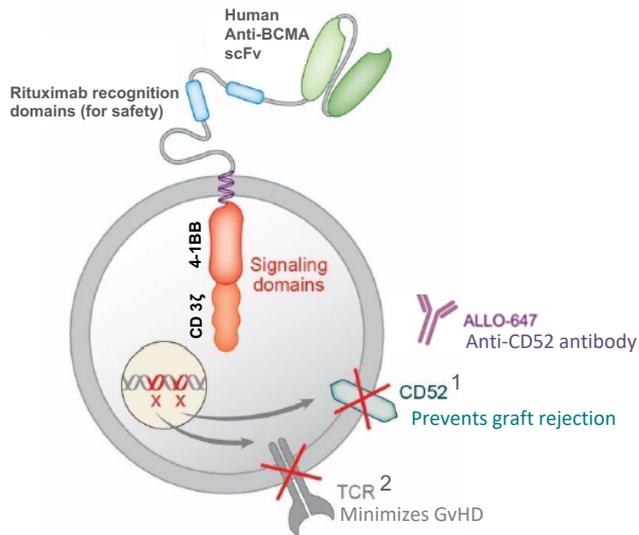
⁵ Sarah Cannon Research Institute at St. David's South Austin Medical Center, Austin, TX; ⁶ Banner MD Anderson Cancer Center, Gilbert, Arizona; ⁷ Vanderbilt University Medical Center, Nashville, TN;

⁸ Allogene Therapeutics, South San Francisco, CA; ⁹ Division of Hematology Oncology, Medical College of Wisconsin, Milwaukee, WI

The First Allogeneic BCMA CAR T Study for R/R Multiple Myeloma

Autologous BCMA cell therapy has demonstrated unprecedented efficacy, but logistics, wait time and need for bridging treatment may limit access

- Allogeneic therapy overcomes these challenges with
 - Potential to treat all eligible patients on demand within days; no need for bridging therapy
 - Scalable manufacturing with less product variability
 - Convenience of repeat dosing
 - Manufacturing amenable to complex engineering, suitable for BCMA platform



1. TALEN-mediated CD52 KO allows selective lymphodepletion with ALLO-647
2. TALEN-mediated TRAC KO eliminates TCR α expression to minimize risk of GvHD



UNIVERSAL: First Allogeneic BCMA CAR T in Multiple Myeloma

Phase 1, Open-label, Multicenter Dose Escalation Study
Enrolling in Eleven US Centers

Key Eligibility Criteria

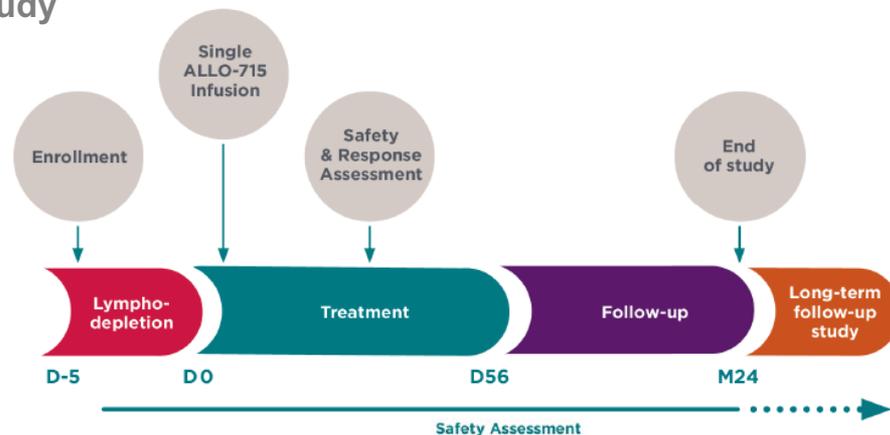
- Relapsed/Refractory Multiple Myeloma
- ≥ 3 prior therapies including IMiD, proteasome inhibitor & anti-CD38
- Refractory to last prior therapy
- ECOG 0 or 1
- No donor-specific antibodies
- No bridging therapy allowed

Primary Endpoints

- Safety and tolerability

Secondary Endpoints

- Recommended ALLO-715 P2 dose and lymphodepletion regimen
- Anti-tumor activity (ORR, duration of response, PFS, and MRD)
- ALLO-715 cellular kinetics (blood levels of anti-BCMA CAR T cells)
- ALLO-647 pharmacokinetics (serum ALLO-647 concentrations)



ALLO-715 Dose Escalation: 40, 160, 320, 480 x 10 ⁶ CAR ⁺ T cells	
Lymphodepletion Regimens (FCA [†] , CA [†])	Doses
Fludarabine	30 mg/m ² /day x 3 days
Cyclophosphamide	300 mg/m ² /day x 3 days
ALLO-647	13 to 30 mg x 3 days

* FCA conditioning with fludarabine, cyclophosphamide and ALLO-647

† CA conditioning with cyclophosphamide and ALLO-647



Patient Flow

Median Time from Enrollment to Start of Treatment: **5 Days**

Enrolled (N=35)

4 patients became ineligible due to organ failures from rapidly progressing disease

Safety Population (N=31)

5 treated patients yet to reach assessment

Efficacy Population (N=26)

CAR ⁺ T Cell Dose	Lymphodepletion Regimen		
	FCA		CA
	Low Dose ALLO-647	High Dose ALLO-647	Low Dose ALLO-647
40 x 10 ⁶ Cells	3	–	–
160 x 10 ⁶ Cells	4	–	3
320 x 10 ⁶ Cells	6	4	3
480 x 10 ⁶ Cells	3	–	–

Overall median follow-up time = **3.2 Months**



Heavily Pretreated Patients with Advanced, Refractory Stage Disease

Characteristics		Safety Population (N = 31)
Age, median (range), years		65 (46, 76)
Gender, %	Male	61
	Female	39
ECOG, %	0	48
	1	52
ISS Stage ≥ 2 , %		74
High-risk cytogenetics*, %		48
Extramedullary disease, %		23
High tumor burden†, %		39
Time since initial diagnosis, median (range), years		5.4 (0.9, 20.1)
Number of prior anti-myeloma regimens, median (range)		5 (3 – 11)
Prior autologous SCT, %		94
Penta-exposed, %		94

* High risk cytogenetics is defined as del 17p, t(4;14), and t(14;16)

† High tumor burden consider when more than 50% plasma cells in bone marrow

- Patients had advanced disease
 - All patients refractory to last line
 - 48% of patients had high-risk cytogenetics
 - 23% of patients had extramedullary disease
- Heavily pretreated patients in study
 - Median of 5 prior lines of therapy
 - 94% patients were penta-exposed



ALLO-715 and ALLO-647 Demonstrated Manageable Safety Profile

AE of Interest* (N=31)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	All Grades
	n (%)					
Cytokine Release Syndrome [†]	5 (16)	9 (29)	–	–	–	14 (45)
ICANS [‡]	–	–	–	–	–	–
Graft-versus-Host Disease	–	–	–	–	–	–
Infection [‡]	2 (7)	6 (19)	4 (13)	–	1 (3)	13 (42)
Infusion Reaction to ALLO-647	4 (13)	3 (10)	–	–	–	7 (23)

- No GvHD, or ICANS
- Manageable CRS; low use of tocilizumab (19%) and steroids (10%)
- Infusion reactions were low grade and manageable
- AEs ≥ grade 3 reported as SAEs occurred in 19% of patients
- Single grade 5 event related to progressive myeloma and conditioning regimen with cyclophosphamide and ALLO-647 (CA cohort)

* Number of patients with AE occurring from the start of study drug up to subsequent anti-cancer therapy. For patients reporting more than one AE within a preferred term, only one AE with the maximum grade is reported.

† ASTCT Lee, 2019. ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome

‡ All infections (bacterial, fungal, and viral) included



Efficacy of ALLO-715 and ALLO-647*

Increasing ORR and VGPR+ rate observed at 320M

Cell Dose & LD Regimen	FCA						CA	
	DL1 (40M)	DL2 (160M)	DL3 (320M)			DL4 (480M)	DL2 (160M)	DL3 (320M)
	Low ALLO-647 (N=3)	Low ALLO-647 (N=4)	Low ALLO-647 (N=6)	High ALLO-647 (N=4)	ALL ALLO-647 (N=10)	Low ALLO-647 (N=3)	Low ALLO-647 (N=3)	
ORR [†] , n (%)	–	2 (50)	3 (50)	3 (75)	6 (60)	1 (33)	–	2 (67)
VGPR+ Rate [†] , n (%)	–	1 (25)	3 (50)	1 (25)	4 (40)	–	–	1 (33)

- ORR achieved in 6 (60%) patients with 4 (40%) VGPR+ rate for the FCA 320M cell dose group
- 5 of the 6 VGPR+ patients have been assessed for MRD status and all were negative

VGPR+ = sCR, CR, or VGPR

*Clinical response evaluation was based on IMWG response criteria, Kumar et al, 2016

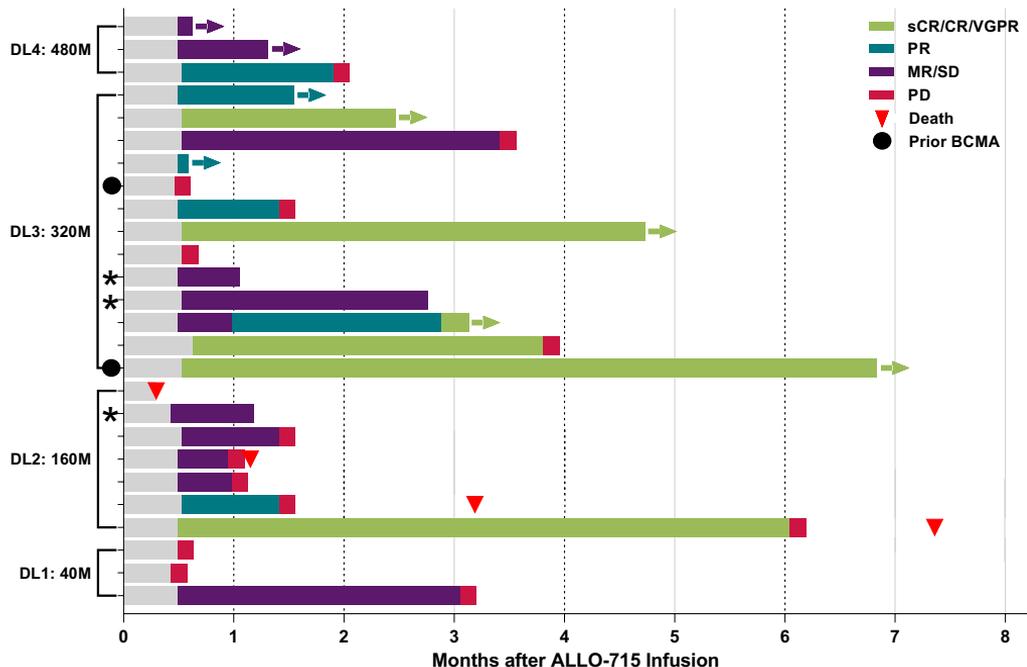
†Responses included 2 subjects with only day 14 assessment and 1 subject who converted from a confirmed PR to VGPR (pending confirmation).

All first responses as of the data-cutoff date have converted to confirmed responses.



Objective Responses are Cell Dose-Dependent

Tumor Response to Study Treatment

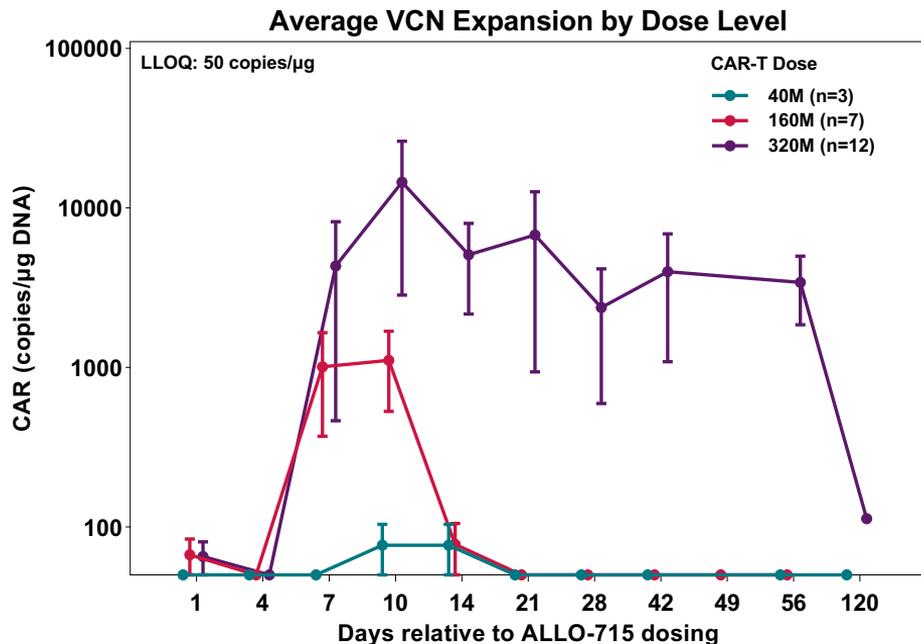


- Median time to response was 16 days
- Increasing response rates as cell dose increases
- 6 out of 9 patients treated with DL3 or DL4 with response remain in response

*Discontinued follow-up on study prior to disease progression.



AlloCAR T Cell Expansion Increased with ALLO-715 Dose Level



- Cell expansion was observed as early as 7 days
- Improved expansion in patients who received higher cell doses
- Persistence observed out to month 4 in dose level 3
- Patients with CAR T expansion had higher serum levels of IL15 at day 0 and day 14 [data not shown]

As of data cutoff date, limited DL4 vector copy number (VCN) data was available (2 patients with neither patient reaching day 28). Remaining data pending.

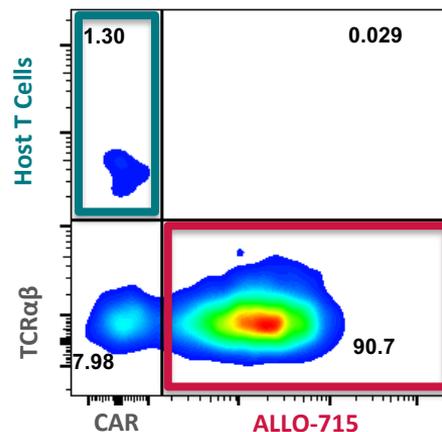


AlloCAR T Cell Expansion Occurs During the Lymphodepletion Window

Patient Case Study

- 71-year-old Caucasian male
- Initially diagnosed with MM in 2014; ISS Stage 2, R-ISS Stage 2
- 9 prior lines of therapy, including auto-SCT and an experimental BCMA targeted therapy and progressing on last line of therapy
- Conditioned with FCA low dose ALLO-647 and received 320M ALLO-715 cells
- Experienced grade 1 CRS with symptoms of fever and tachycardia, treated with acetaminophen
- Achieved a VGPR on day 14 which deepened to a sCR by day 28

Flow plot of Patient Lymphocytes on D14

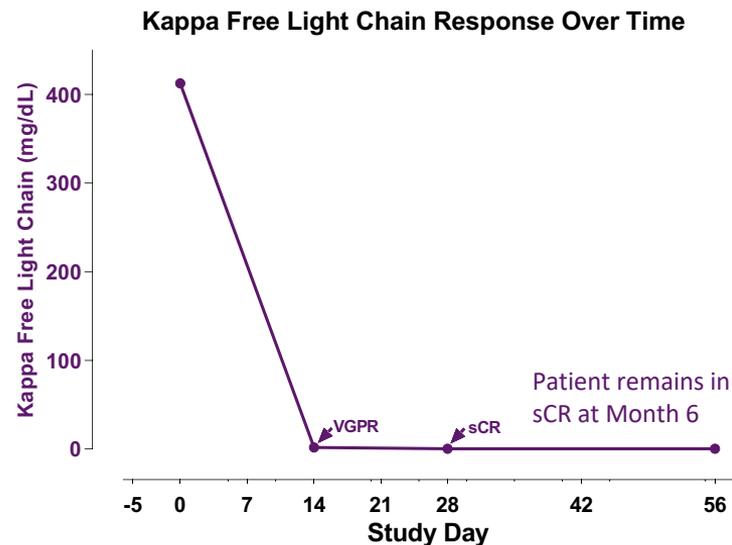
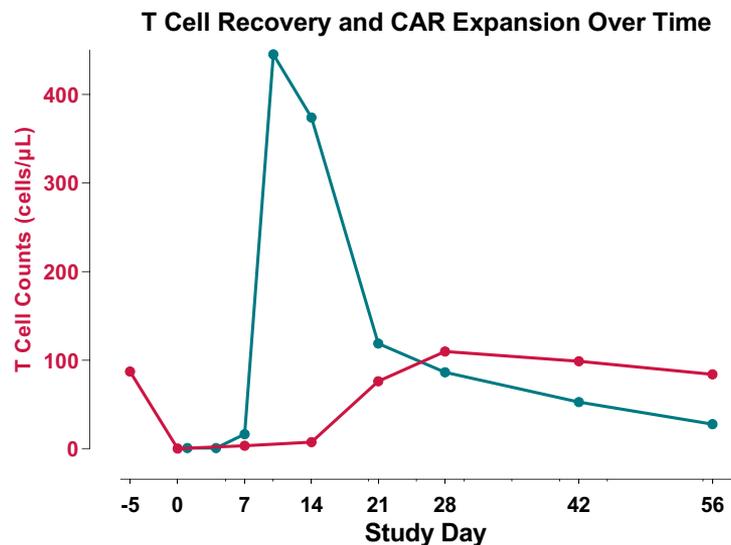


91% of patient lymphocytes are CAR+ by Day 14



Kinetics of AlloCAR T Cell Persistence, Lymphocyte Count and Response

Patient Case Study



Summary

These results demonstrate feasibility of “off the shelf” CAR T in Multiple Myeloma

- UNIVERSAL is the first allogeneic BCMA CAR T trial presented
 - Approximately 90% of patients were treated within 5 days of study enrollment
 - No bridging therapy required prior to ALLO-715 dosing
- ALLO-715 and ALLO-647 regimens were well tolerated across all dose levels
 - No GVHD or neurotoxicity (ICANS) and manageable grade 1 or 2 CRS
 - Infection rate similar to other studies in advanced multiple myeloma
- Dose dependent ALLO-715 activity observed in heavily pretreated, refractory patients
 - Expansion and persistence of ALLO-715 cells observed through month 4
 - 320M cell dose of ALLO-715 (DL3) with FCA associated with a 60% Overall Response Rate (ORR)
 - 5 of the 6 VGPR+ patients assessed for MRD status and all were negative
- Ongoing enrollment for planned evaluation of higher cell-doses and lymphodepletion



THANK YOU

To Patients, their families and caregivers,
Clinical Trial Investigators and Sites

ALLO-715 (BCMA) utilizes TALEN® gene-editing technology pioneered and owned by Collectis. Allogene has an exclusive license to the Collectis technology for allogeneic products directed at this target and holds all global development and commercial rights for this investigational candidate.



Disclosure

Sham Mailankody has received research support for clinical trials from Juno Therapeutics, Janssen Pharmaceuticals, Takeda, and Allogene Therapeutics. He has received honoraria from Physicians' Education Resource.

