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)

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Presented by Sham Mailankody, MBBS
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 TCRα 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

<table>
<thead>
<tr>
<th>Lymphodepletion Regimens (FCA*, CA†)</th>
<th>Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fludarabine</td>
<td>30 mg/m^2/day x 3 days</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>300 mg/m^2/day x 3 days</td>
</tr>
<tr>
<td>ALLO-647</td>
<td>13 to 30 mg x 3 days</td>
</tr>
</tbody>
</table>

* 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)

<table>
<thead>
<tr>
<th>CAR+ T Cell Dose</th>
<th>Lymphodepletion Regimen</th>
<th>CA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FCA</td>
<td>CA</td>
</tr>
<tr>
<td>Low Dose ALLO-647</td>
<td>High Dose ALLO-647</td>
<td></td>
</tr>
<tr>
<td>40 x 10^6 Cells</td>
<td>3</td>
<td>–</td>
</tr>
<tr>
<td>160 x 10^6 Cells</td>
<td>4</td>
<td>–</td>
</tr>
<tr>
<td>320 x 10^6 Cells</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>480 x 10^6 Cells</td>
<td>3</td>
<td>–</td>
</tr>
</tbody>
</table>

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

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

* 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

- 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)

<table>
<thead>
<tr>
<th>AE of Interest* (N=31)</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
<th>All Grades</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Cytokine Release Syndrome†</td>
<td>5 (16)</td>
<td>9 (29)</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>14 (45)</td>
</tr>
<tr>
<td>ICANS†</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Graft-versus-Host Disease</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Infection‡</td>
<td>2 (7)</td>
<td>6 (19)</td>
<td>4 (13)</td>
<td>−</td>
<td>1 (3)</td>
<td>13 (42)</td>
</tr>
<tr>
<td>Infusion Reaction to ALLO-647</td>
<td>4 (13)</td>
<td>3 (10)</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>7 (23)</td>
</tr>
</tbody>
</table>

* 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

<table>
<thead>
<tr>
<th>Cell Dose &amp; LD Regimen</th>
<th>FCA</th>
<th>CA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DL1 (40M)</td>
<td>DL2 (160M)</td>
</tr>
<tr>
<td>Low ALLO-647 (N=3)</td>
<td>-</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Low ALLO-647 (N=4)</td>
<td>-</td>
<td>3 (50)</td>
</tr>
<tr>
<td>Low ALLO-647 (N=6)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>High ALLO-647 (N=4)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>ALLO-647 (N=10)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Low ALLO-647 (N=3)</td>
<td>2 (50)</td>
<td></td>
</tr>
<tr>
<td>Low ALLO-647 (N=3)</td>
<td>3 (50)</td>
<td></td>
</tr>
<tr>
<td>Low ALLO-647 (N=3)</td>
<td>1 (25)</td>
<td></td>
</tr>
</tbody>
</table>

**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)

VGPR+ = sCR, CR, or VGPR

- 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

*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

- 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

Tumor Response to Study Treatment

- Data Cutoff Date: October 30, 2020

*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

T Cell Recovery and CAR Expansion Over Time

Kappa Free Light Chain Response Over Time

Patient remains in sCR at Month 6
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 Cellectis. Allogene has an exclusive license to the Cellectis technology for allogeneic products directed at this target and holds all global development and commercial rights for this investigational candidate.
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.