UNIVERSAL Updated Phase 1 Data Highlight Role of Allogeneic Anti-BCMA ALLO-715 Therapy for Relapsed/Refractory Multiple Myeloma


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Background
- Autologous chimeric antigen receptor (CAR) T therapies have advanced the treatment of relapsed/refractory multiple myeloma (RR-MM).1
- Due to access and treatment delays, many patients may not benefit from these therapies. Allogeneic CAR T cell products may address access challenges and enhance eligible patients benefits.2

- ALLO-715 is a genetically modified anti-cell reactivation antigen (BCMA) Allogene CAR T cell therapy that uses TALEN® technology to disrupt the T-cell receptor alpha constant (TRAC) and the CD52 genes.
- The goal of intervention with ALLO-715 is to eliminate the risk of graft-versus-host disease (GvHD) and permit the use of ALLO-647, an anti-CD52 monoclonal antibody (mAb), for selective and transitory lymphodepletion (LD).
- UNIVERSAL is an open-label, multicenter (13 US centers), Phase 1 trial (NCT04093596)

Methods
- **Primary Endpoints**
  - Safety and dose-limiting toxicity (DLT)

- **Secondary Endpoints**
  - Recommended ALLO-715 Phase 2 dose and LD regimen
  - Anti-tumor activity (ORR, duration of response, PFS, and MTD)

- **DL3** cellular kinetics (blood levels of anti-BCMA CAR T cells)
- ALLO-647 pharmacokinetics (serum ALLO-647 concentrations)

- **Study Population**
  - As of October 11, 2022, 59 patients were enrolled; 54 received LD and were treated with ALLO-715. 1 became ineligible due to organ failure from rapid progressive disease.
  - Patients had advanced disease following prior therapy (Table 1).

Table 1. Patient Demographics, Disease Status, and Prior Therapies in DL3 Expansion

<table>
<thead>
<tr>
<th>Category</th>
<th>DL3 (N=28)</th>
<th>FCA39 (n=17)</th>
<th>FCA60 (n=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), yrs</td>
<td>65 (49, 78)</td>
<td>66 (57, 77)</td>
<td>65 (49, 78)</td>
</tr>
<tr>
<td>Prior Autologous SCT, %</td>
<td>50 / 50</td>
<td>55 / 46</td>
<td>57 / 53</td>
</tr>
<tr>
<td>ISS Stage III, %</td>
<td>25 27</td>
<td>25 29</td>
<td>27 30</td>
</tr>
<tr>
<td>Extramedullary Disease, %</td>
<td>29 36</td>
<td>36 24</td>
<td>29 36</td>
</tr>
<tr>
<td>ALLO-647 dose regimen</td>
<td>7.2 (1, 26)</td>
<td>6.1 (2, 20)</td>
<td>8.3 (2, 26)</td>
</tr>
<tr>
<td>Prior Myeloma Episodes, median, yrs</td>
<td>6 (1, 15)</td>
<td>8 (1, 15)</td>
<td>6 (1, 15)</td>
</tr>
<tr>
<td>Prior allogeneic CAR T, %</td>
<td>39 31</td>
<td>35 29</td>
<td>36 31</td>
</tr>
<tr>
<td>Cytokine Release Syndrome (%)</td>
<td>36 24</td>
<td>36 24</td>
<td>36 24</td>
</tr>
<tr>
<td><strong>Efficacy Results</strong></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
| Twenty-eight patients received DL3 at FCA39 or FCA60 with 23 patients included in the efficacy-evaluable population.3
- Five patients followed for less than 3 months are not included due to limited follow-up, with responses ranging from 0% to PR.

Table 2. Adverse Events of Special Interest (Safety Analysis Set)

<table>
<thead>
<tr>
<th>AE Category</th>
<th>Grade 1/2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gr 5 Infections</strong></td>
<td>25 (46)</td>
<td>10 (19)</td>
<td>1 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Cytokine Release Syndrome</strong></td>
<td>7 (13)</td>
<td>9 (17)</td>
<td>13 (24)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Table 3. Responses in Efficacy Evaluable Patients Followed ≥3 Months

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORR</strong></td>
<td>7 (46)</td>
<td>8 (47)</td>
<td>15 (50)</td>
</tr>
<tr>
<td><strong>VGPR</strong></td>
<td>6 (54)</td>
<td>5 (42)</td>
<td>11 (38)</td>
</tr>
<tr>
<td><strong>CR</strong></td>
<td>25 (91)</td>
<td>15 (72)</td>
<td>27 (93)</td>
</tr>
<tr>
<td><strong>CR with MRD Neg</strong></td>
<td>5 (21)</td>
<td>9 (45)</td>
<td>13 (44)</td>
</tr>
<tr>
<td><strong>MRD</strong></td>
<td>6 (36)</td>
<td>2 (10)</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>
| **Median DOR**            | 8, 44  | 8, 44  | 8, 44  |}

Conclusions
- **Safety Results**
  - Cytokine release syndrome (CRS) occurred in 52% of patients, all were Gr 1/2 except one Gr 3.
  - The use of busulphan and steroids across all patients was 24% and 17%, respectively.

- **Efficacy Results**
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For questions or comments, please email majekodun@medsci.org

Data Cut-off Date: October 15, 2022