Durable Responses Achievable with Anti-CD19 Allogeneic CAR T ALLO-501/501A in Phase 1 Trials of Autologous CAR T-Naive Patients with Relapsed/Refractory Large B-Cell Lymphoma (r/r LBCL)


Munoz Clinic Comprehensive Cancer Center, Phoenix, AZ; Moffitt Cancer Center, Tampa, FL; University of Miami, Miami, FL; Ronald Reagan UCLA Medical Center, Los Angeles, CA; Colorado Blood Cancer Institute, Denver, CO; VCU VCUHG, Los Angeles, CA; Banner Health Center, Gilbert, AZ; North Carolina Cancer Institute, Louisville, KY; North Cancer Transplant & Cellular Therapy Program at St. David’s South Austin Medical Center, Austin, TX; Yale College of Medicine at New Haven, New Haven, CT; Memorial University of Newfoundland, St. John’s, NL; Thomas Jefferson University Cancer Center, New York, NY; Stanford University, Stanford, CA;

*Allogeneic Therapeutics, San Francisco, CA; **The University of Texas M.D. Anderson Cancer Center, Houston, TX.

Background
- Autologous CAR T cell therapies have transformed the treatment of relapsed/refractory non-Hodgkin lymphoma (rr NHL) but, due to a lengthy and cumbersome manufacturing processes, are not available to all eligible patients (pts).
- ALLO-501A is an HLA-unmatched, off-the-shelf, investigational, anti-CD19 allogeneic CAR T cell product administered as a one-time treatment that is potentially capable of inducing durable remissions in rr LBCL. pts. ALLO-501A is similar to ALLO-501A for the inclusion of a rituximab switch.
- Two studies, ALPHIA (NCT03393026) and ALPH2A (NCT04149884), were undertaken to evaluate ALLO-501A and ALLO-501A in pts with rr NHL.
- This update focuses on a subgroup of pts from the ALPHIA and ALPH2A studies who were treated with the regimen currently being evaluated in ALPH2A, a potentially pivotal Phase 2 trial in pts with rr LBCL.

Baseline Patient and Disease Characteristics
- Pts were heavily pretreated and had unfavorable baseline disease characteristics.
- Two thirds of pts had stage IV disease and two thirds had an elevated LDH at time of study enrollment.
- 92% of pts had an ECOG Performance Status (PS) of 1.
- Half or more of the pts had an IP score >2, extranodal disease, and/or prior hematopoietic cell transplant.
- One third of pts had double or triple hit lymphomas.

<table>
<thead>
<tr>
<th>Table 1. Baseline Patient Characteristics</th>
<th>n (%)</th>
<th>Pts Treated With Phase 2 Regimen (N=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All CAR T-Naive (N=13)</strong></td>
<td>60 years</td>
<td>66%</td>
</tr>
<tr>
<td>Stage IV disease</td>
<td>92%</td>
<td>50%</td>
</tr>
<tr>
<td>ECOG PS of 1</td>
<td>92%</td>
<td>50%</td>
</tr>
<tr>
<td>Baseline LDH &gt; ULN</td>
<td>87%</td>
<td>50%</td>
</tr>
<tr>
<td>IP score &gt;2</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Terminal center subtype</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Double or triple hit</td>
<td>33%</td>
<td>33%</td>
</tr>
<tr>
<td>Median prior regimens</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Prior transplant</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Extramedullary disease</td>
<td>58%</td>
<td>58%</td>
</tr>
</tbody>
</table>

Methods

Subgroup Selection and Analysis Sets
- CAR T-naive pts with rr LBCL (N=13) were treated with escalating doses of ALLO-501A/501A manufactured with the Phase 2 process after lymphodepletion with FC and varying doses of ALLO-647. This subgroup comprises the safety set.
- Based on the overall Phase 1 experience, lymphodepletion with FC and a single infusion of ALLO-501A was selected for evaluation in the Phase 2 portion of ALPH2A.
- 12 of the 13 pts in the safety set received lymphodepletion with FC/ALLO-647, the selected Phase 2 lymphodepletion regimen. These patients comprise the efficacy and translational analysis set.

Endpoints
- Safety, tolerability, efficacy (overall response rate [ORR], complete response [CR] rate, and duration of response [DOR])
- T cell kinetics as measured by transgene levels in the peripheral blood
- Leukocyte recovery

Treatment Experience and Follow Up
- All treated pts (100%) received study treatment as intended, each infused dose of allogeneic CAR T cells was manufactured and released per production specifications.
- 3-day median time from enritment to initiation of study treatment.
- No patients required bridging therapy.
- The median follow-up was 32.9 months.

Safety and Tolerability
- No Gr3-3 CRS events or any ICANS events were observed.
- No GVHD events were reported.
- Infections included lower-grade viral reactivations detected on weekly protocol-required surveillance. Infections were manageable with routine treatment; no fatal infections were observed.
- Adverse events with FC/ALLO-647 lymphodepletion were consistent with those in the full subgroup.

Efficacy
- The ORR was 67% and the CR rate was 58%, with a median duration of response of 23.1 months.

<p>| Table 3. Response Rates in Pts Treated With Selected Phase 2 Regimen |
|---|---|---|
| n (%) | Pts Treated With Phase 2 Regimen (N=12) |</p>
<table>
<thead>
<tr>
<th>ORR</th>
<th>CR</th>
<th>5-month CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (67)</td>
<td>7 (58)</td>
<td>5 (42)</td>
</tr>
</tbody>
</table>

Conclusions

- A single dose of ALLO-501A/501A following FC/ALLO-647 provided durable remissions up to 31 months that compared favorably to outcomes achieved with autologous CAR T cell therapies in pts with rr LBCL.
- ALLO-501A/501A following FC/ALLO-647 was generally well tolerated with only low-grade CRS, no ICANS, and no GVHD.
- Cytopenias and infections were manageable and comparable to experience with autologous CAR T cell therapies in rr LBCL.
- Selective lymphodepletion with FC/ALLO-647 creates a window for ALLO-501A/501A enrollment, persistence, and anti-tumor activity.
- ALLO-501A, as an off-the-shelf, allogeneic CAR T cell product, eliminates the need for leukapheresis or bridging therapy, and may be more accessible to all eligible patients seeking CAR T therapy.
- These findings support broader evaluation of ALLO-501A with the selected Phase 2 regimen in the first, potentially pivotal Phase 2 trials (ALPH2A, NCT03393026, and EXPAND, NCT07143345) of an allogeneic CAR T cell product.

Acknowledgments: ALLO-501A/501A are anti-CD19 allogeneic CAR T (AlloCAR T™) therapies being jointly developed under a collaboration agreement between Bellicum and Allogene based on an exclusive license granted by Cellectis to Bellicum. ALLO-CAR T uses Cellectis technologies. Servier grants to Allogene exclusive rights to ALLO-501A/501A in the U.S., while Servier retains exclusive rights for all other countries.

For questions or comments, please e-mail Munoz.Jhon@asmp.org.

Elka Czajkowska, April 20, 2023.