Phase 1 Results with Anti-CD12 Allogeneic CAR T ALLO-501/501A in Relapsed/Refractory Large B-Cell Lymphoma (r/r LBCL)

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Background

- Autologous CAR T cell therapies have transformed the treatment of relapsed/refractory non-Hodgkin lymphoma (r/r NHL) but, due to a lengthy and cumbersome manufacturing processes, are not available to all eligible patients (pts).
- ALLO-501 is an sHLA-unnatched, off-the-shelf, investigational, anti-CD12 allogeneic CAR T cell product administered as a one-time treatment that is potentially capable of inducing durable remissions in r/r LBCL, a disease similar to ALLO-501A, except for the inclusion of a ruxutamib switch off.
- Two studies, ALPHAC (NCT03939026) and ALPHAZ (NCT04641968), were undertaken to evaluate ALLO-501 and ALLO-501A in pts with r/r NHL.
- This update focuses on a subgroup of 33 pts from the ALPHAC and ALPHAZ studies who were treated with the regimen currently being evaluated in ALPHAZ2, a potentially pivotal Phase 2 trial in pts with r/r LBCL.

Methods

Subgroup Selection and Analysis Sets
- CAR T-naive pts with r/r LBCL (N=33) were treated with escalating doses of ALLO-501/501A 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 FC60 and a single infusion of ALLO-501A was selected for evaluation in the Phase 2 portion of ALPHAZ.
- 12 of the 33 pts in the safety set received lymphodepletion with FC60, 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, duration of response [DOR])
- T cell kinetics as measured by transgene levels in the peripheral blood
- Leukostasis recovery

Baseline Patient and Disease Characteristics

- 3 pts were heavily pretreated and had unfavorable baseline disease characteristics.
- Two of the pts had stage IV disease and two 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 IPI score ≥2, extranodal disease, and/or prior hematopoetic cell transplant.
- One third of pts had double or triple hit lymphomas.

Table 1. Baseline Patient Characteristics

<table>
<thead>
<tr>
<th>Trait</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range)</td>
<td>69 (26-82)</td>
</tr>
<tr>
<td>Stage IV disease</td>
<td>92%</td>
</tr>
<tr>
<td>Baseline LDH = ULN</td>
<td>50%</td>
</tr>
<tr>
<td>IPI score ≥2</td>
<td>50%</td>
</tr>
<tr>
<td>Extramedial disease</td>
<td>50%</td>
</tr>
</tbody>
</table>

Figure 1. ALLO-501/501A

Safety and Tolerability

- No Gr 3/4 CRS events or any ICANS events were observed.
- No GVHD events were reported.
- Infections included low-grade viral reactivations detected on weekly protocol-required surveillance. Infections were manageable with standard of care treatment.
- No adverse events with FC60 lymphodepletion were consistent with those in the full study population.

Table 2. Adverse Events of Interest

<table>
<thead>
<tr>
<th>Event</th>
<th>ALLO-501 (n=32)</th>
<th>ALLO-501A (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRS</td>
<td>8 (24)</td>
<td>0</td>
</tr>
<tr>
<td>GvHD</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neurotoxicity</td>
<td>13 (38)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>ESRD</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Infection</td>
<td>19 (58)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Protocol</td>
<td>4 (12)</td>
<td>- (0)</td>
</tr>
</tbody>
</table>

Figure 2. Dosing & Administration With Selected Phase 2 Treatment Regimen

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 product specifications.
- 3 day median time from enrollment to initiation of study treatment.
- No patients required bridging therapy.
- The median follow-up was 32.9 months.

Baseline Disease Characteristics

- The ORR was 86% and the CR rate was 58%, with a median duration of response of 23.1 months.

Table 3. Response Rates in Pts Treated With Phase 2 Regimen (N=21)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>ORR (%)</th>
<th>CR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pts Treated With Phase 2 Regimen (N=21)</td>
<td>8 (6/7)</td>
<td>5 (42)</td>
</tr>
</tbody>
</table>

Figure 5. Leukostat Count Recovery With Selected Phase 2 Treatment Regimen

Safety and Tolerability

- No neutrophils recovered at a median of 7 days after ALLO-501A.
- Lymphocytes recovered at a median of 21 days after ALLO-501A.

Translational Analyses

CAR T Cell Expansion
- Calculated AUC (log of copies per microgram of DNA) per subject was markedly higher in peripheral blood sampled from Day 1 through Day 28 among responders vs non-responders.
- Allogeneic CAR T cell peak expansion and persistence was higher in responders vs non-responders (log of copies per microgram of DNA).

Figure 4. ALLO-501/501A CAR T Cell Expansion Is Associated With Response (N=11)

Conclusions

- A single dose of ALLO-501/501A following FAC90 provided durable remissions up to 31 months that compared favorably to outcomes achieved with autologous CAR T cell therapies in patients with r/r LBCL.
- ALLO-501/501A following FAC90 was generally well tolerated with only low-grade CRS, no ICANS, and no GVHD.
- Cytophenias and infections were manageable and comparable to experience with autologous CAR T cell therapies in r/r LBCL.
- Selective lymphodepletion with FAC90 creates a window for ALLO-501/501A engraftment, persistence, and anti-tumor activity.
- ALLO-501A, as an off-the-shelf, allogeneic CAR T cell product, eliminates the need for leukostasis 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 ongoing, first-in-patients Phase 2 trials (ALPHAC, NCT03939026, and EXPAND, NCT07514345) of an allogeneic CAR T cell product.

Acknowledgments: ALLO-501/501A are the anti-CD12 allogeneic CAR T (ALLO-501) therapies being jointly developed under a collaboration agreement between Servier and Allogene based on an exclusive license granted by Collectix in Servier: ALLO-501/501A uses Collectix technologies. Servier grants to Collectix exclusive rights to ALLO-501/501A in the U.S. while Collectix retains the exclusive rights for all other countries.

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