First-in-Human Data of ALLO-501 and ALLO-647 in Relapsed/Refractory Large B-cell or Follicular Lymphoma (R/R LBCL/FL): ALPHA Study

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Allogeneic CAR T Cell Therapy for R/R Non-Hodgkin Lymphoma

Allogeneic CAR T therapy may provide the benefits of autologous CAR T therapy while addressing challenges:

- **Access**
  - Potential to treat all eligible patients
  - Convenience of repeat dosing
  - No need for complex logistics
- **Speed/Reliability**
  - "Off the shelf" treatment
  - Less product variability, made from healthy T cells

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

Murine CD19 (4G7) scFv
Rituximab recognition domains

TALEN® is a Cellectis gene editing technology
ALPHA Study (NCT03939026) Design and Endpoints
Phase 1, Open-label, Multicenter Dose Escalation Study

Primary Endpoints
• Safety and dose-limiting toxicity of ALLO-647/Flu/Cy followed by ALLO-501

Key Secondary Endpoints
• Overall response rate
• ALLO-501 cell kinetics
• ALLO-647 PK

Key Eligibility Criteria
• R/R LBCL or FL
• At least 2 prior lines of therapy, including an anti-CD20 monoclonal antibody
• ECOG 0 or 1
• Prior autologous CAR T allowed if tumor remains CD19+
• Patients with Donor Specific Antibodies and rituximab > 15ng/ml were excluded

### Cell Dose

<table>
<thead>
<tr>
<th></th>
<th>DL1</th>
<th>DL2</th>
<th>DL3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell Dose</td>
<td>40 x 10⁶ CAR⁺ T cells</td>
<td>120 x 10⁶ CAR⁺ T cells</td>
<td>360 x 10⁶ CAR⁺ T cells</td>
</tr>
</tbody>
</table>

• Lymphodepletion Regimens
  • LD1: Flu/Cy and ALLO-647 13 mg/d x 3 days
  • LD2/LD3: Flu/Cy and ALLO-647 30 mg/d x 3 days (concomitant/staggered)

Fludarabine (Flu): 30 mg/m²/d x 3 days  Cyclophosphamide (Cy): 300 mg/m²/d x 3 days
# ALPHA Phase 1 Patient Characteristics

### Number (%) of patients

<table>
<thead>
<tr>
<th></th>
<th>40 x 10^6 DL 1 (N=4)</th>
<th>120 x 10^6 DL 2 (N=10)</th>
<th>360 x 10^6 DL 3 (N=8)</th>
<th>All Patients (N=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age, years (range)</td>
<td>57 (42, 67)</td>
<td>70 (37, 73)</td>
<td>54 (34, 67)</td>
<td>63 (34, 73)</td>
</tr>
<tr>
<td>Male</td>
<td>3 (75%)</td>
<td>8 (80%)</td>
<td>6 (75%)</td>
<td>17 (77%)</td>
</tr>
</tbody>
</table>

### Lymphoma Subtypes

<table>
<thead>
<tr>
<th></th>
<th>40 x 10^6 DL 1 (N=4)</th>
<th>120 x 10^6 DL 2 (N=10)</th>
<th>360 x 10^6 DL 3 (N=8)</th>
<th>All Patients (N=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse Large B-cell Lymphoma †</td>
<td>3 (75%)</td>
<td>5 (50%)</td>
<td>6 (75%)</td>
<td>14 (64%)</td>
</tr>
<tr>
<td>Follicular Lymphoma</td>
<td>1 (25%)</td>
<td>5 (50%)</td>
<td>2 (25%)</td>
<td>8 (36%)</td>
</tr>
</tbody>
</table>

### Current Disease Stage (per Lugano 2014) #

<table>
<thead>
<tr>
<th></th>
<th>40 x 10^6 DL 1 (N=4)</th>
<th>120 x 10^6 DL 2 (N=10)</th>
<th>360 x 10^6 DL 3 (N=8)</th>
<th>All Patients (N=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage III</td>
<td>1 (25%)</td>
<td>5 (50%)</td>
<td>2 (25%)</td>
<td>8 (36%)</td>
</tr>
<tr>
<td>Stage IV</td>
<td>2 (50%)</td>
<td>5 (50%)</td>
<td>6 (75%)</td>
<td>13 (59%)</td>
</tr>
<tr>
<td>FL(IPI) Score 3-5</td>
<td>1 (25%)</td>
<td>6 (60%)</td>
<td>5 (63%)</td>
<td>12 (55%)</td>
</tr>
</tbody>
</table>

### Prior Treatments

<table>
<thead>
<tr>
<th></th>
<th>40 x 10^6 DL 1 (N=4)</th>
<th>120 x 10^6 DL 2 (N=10)</th>
<th>360 x 10^6 DL 3 (N=8)</th>
<th>All Patients (N=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Number (range)</td>
<td>2 (2-4)</td>
<td>4 (3-4)</td>
<td>5 (3-8)</td>
<td>4 (2-8)</td>
</tr>
<tr>
<td>Hematopoietic Stem Cell Transplant</td>
<td>2 (50%)</td>
<td>4 (40%)</td>
<td>3 (38%)</td>
<td>9 (41%)</td>
</tr>
<tr>
<td>Autologous CAR T cell</td>
<td>-</td>
<td>1 (10%)</td>
<td>3 (38%)</td>
<td>4 (18%)</td>
</tr>
</tbody>
</table>

- Heavily pretreated patients with advanced-stage disease
- 14 (64%) of patients were chemo refractory*
- 4 patients received prior AutoCAR T
  - 2 had short-lasting PR as best response and 2 had PD as best response with AutoCAR T
- Analyses sets:
  - Efficacy: N=19
  - Safety: N=22

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† Not otherwise specified, transformed FL, high-grade B cell lymphoma (double and triple hit), DLBCL coexistent with FL of any grade
‡ 1 patient with stage II disease treated at DL1
# 1 patient with stage II disease treated at DL1
* Defined as best outcome of SD or PD following last therapy, or progression within 12 months following Hematopoietic Stem Cell Transplant

Data Cutoff Date: May 11, 2020
ALPHA Phase 1 Patient Flow

Enrolled Patients: 23*

1 patient was enrolled but removed before lymphodepletion due to acute kidney injury

Treated Patients: 22

<table>
<thead>
<tr>
<th>CAR+ T cells Dose</th>
<th>39mg ALLO-647</th>
<th>90mg ALLO-647</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 x 10^6 CAR⁺ T cells</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>120 x 10^6 CAR⁺ T cells</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>360 x 10^6 CAR⁺ T cells</td>
<td>3</td>
<td>5</td>
</tr>
</tbody>
</table>

- Efficacy Analysis Set (All patients with at least 1 imaging assessment): 19
- One lot of ALLO-501 used

Median/Mean Time from Enrollment to Start of Lymphodepletion: 5 Days
**ALLO-501 and ALLO-647 Demonstrate Manageable Safety Profile**

### AE of Interest  
<table>
<thead>
<tr>
<th>AE of Interest</th>
<th>Grade 1 n (%)</th>
<th>Grade 2 n (%)</th>
<th>Grade 3 n (%)</th>
<th>Grade 4 n (%)</th>
<th>Grade 5 n (%)</th>
<th>All grades n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytokine Release Syndrome *</td>
<td>2 (9%)</td>
<td>4 (18%)</td>
<td>1 (5%)</td>
<td>-</td>
<td>-</td>
<td>7 (32%)</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>5 (23%)</td>
<td>4 (18%)</td>
<td>2 (9%) ‡</td>
<td>-</td>
<td>-</td>
<td>11 (50%)</td>
</tr>
<tr>
<td>Infusion Reaction #</td>
<td>1 (5%)</td>
<td>9 (41%)</td>
<td>1 (5%)</td>
<td>-</td>
<td>-</td>
<td>11 (50%)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>-</td>
<td>1 (5%)</td>
<td>7 (32%)</td>
<td>7 (32%)</td>
<td>-</td>
<td>15 (68%)</td>
</tr>
</tbody>
</table>

- No DLT, GvHD
- Manageable CRS
- ALLO-501 toxicity not dose-proportional
- Median duration of hospitalization from D0: 7 days

### Serious Adverse Events (time to resolution) ‡

- 4 patients (18%):
  - Gr2 pyrexia (2 days) and Gr2 CMV reactivation (6 days)
  - Gr3 rotavirus infection (15 days) and Gr3 hypokalemia (2 days)
  - Gr3 febrile neutropenia (2 days) and Gr3 hypotension (2 days)
  - Gr3 upper GI hemorrhage (<1 day) and Gr3 CMV reactivation (25 days)

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* ASTCT Lee, 2019. ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome
* CMV reactivations and Rotavirus infection
# attributed to ALLO-647

‡ Number of patients with AE regardless of attribution unless otherwise indicated, 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).

Data Cutoff Date: May 11, 2020
## Phase 1 ALPHA Best Overall Response

<table>
<thead>
<tr>
<th>Cell Dose and LD regimen</th>
<th>39mg ALLO-647</th>
<th></th>
<th>ALL 39mg ALLO-647 (N = 11)</th>
<th>90mg ALLO-647</th>
<th>ALL 90mg ALLO-647 (N=8)</th>
<th>All Patients (N=19) Rate (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 x 10^6 CAR^+ cells (N=4)</td>
<td>40 x 10^6 CAR^+ cells (N=4)</td>
<td>360 x 10^6 CAR^+ cells (N=3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORR, n (%)</td>
<td>3 (75%)</td>
<td>3 (75%)</td>
<td>1 (33%)</td>
<td>7 (64%)</td>
<td>4 (67%)</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>CR, n (%)</td>
<td>1 (25%)</td>
<td>1 (25%)</td>
<td>1 (33%)</td>
<td>3 (27%)</td>
<td>4 (67%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

**Median follow-up time:** 3.8 months (range: 0.7 - 6.1)
Reduction in Tumor Size Observed with ALLO-501

* Received prior AutoCAR T

Data Cutoff Date: May 11, 2020
Nine of Twelve Responders Remain in Response

ALLO-647: 39 mg
Median follow up: 4.3 months (1.0, 6.1)

ALLO-647: 90 mg
Median follow up: 1.9 months (0.7, 2.6)

One patient who progressed after a PR was re-dosed with ALLO-501 (120 x 10^6) and Flu/Cy/90mg ALLO-647 and achieved a CR

* Received prior AutoCAR T

Data Cutoff Date: May 11, 2020

Sattva S. Neelapu, M.D., The University of Texas MD Anderson Cancer Center, Department of Lymphoma/Myeloma, Houston, TX
AlloCAR T Cell Expansion Is Associated with Clinical Response

CAR T Expansion and Persistence

Study Day

CAR Copies/ug DNA

100000
10000
1000
100
10

CR
PR
SD/PD

6
5
4
6
4
4
4
4
6
6
6
5
2
2
1
1

Reference Line - LLOQ
ALLO-647 Mediates Selective Lymphodepletion

- No difference in neutrophil kinetics between ALLO-647 treatment groups
- Median time to Platelet >=100K is 8 days for 90mg ALLO-647 dose cohort
ALLO-501 Patient Case Study

- **120 x 10⁶ CAR⁺ T cells after Flu/Cy + 39mg ALLO-647**
- 70-year-old male with follicular lymphoma
- FLIPI 4, stage 4 (bone marrow infiltration), splenic involvement
- Primary refractory with 4 prior lines of therapy (best outcome)
  1. R-Benda x 4 cycles (PD)
  2. R-CHOP x 2 cycles (SD)
  3. R-Len x 2 cycles (PD)
  4. Copanlisib x 2 cycles (SD)
- Safety:
  - ALLO-647-related: Grade 1 pyrexia

Patient remains in CR at Month 4

Courtesy of Sattva Neelapu
ALLO-501 Patient Case Study:
AlloCAR T Expansion Occurs During Lymphodepletion Window

ALLO-647 PK, CAR Expansion and T Cell Recovery Over Time

Flow Plot of Patient Lymphocytes on D14

Host T Cells (TCRαß⁺, CAR T⁻)

ALLO-501 (TCRαß⁺, CAR T⁺)
Conclusions

- **ALLO-501 and ALLO-647 based lymphodepletion (LD) were well tolerated**
  - No DLT, GvHD or ICANS
  - Manageable CRS and no >Gr3 infections

- **AlloCAR T cell expansion was associated with responses**

- **Anti-tumor activity was observed across all cell dose levels**
  - Overall: ORR observed in 12/19 (63%) patients with 37% CR
  - 9 of the 12 (75%) responding patients remain in response as of the data cutoff
  - 1 patient achieved CR after the 2nd infusion of ALLO-501

- **ALLO-647 delays host T cell recovery**
  - Higher dose ALLO-647 appear to associate with deeper responses (50% CR)

- **Optimization of LD and patient follow-up is ongoing**

- **Phase I trial of ALLO-501A (ALLO-501 minus rituximab switch) is enrolling**
ALLO-501 is an anti-CD19 allogeneic CAR T (AlloCAR T™) therapy being jointly developed under a collaboration agreement between Servier and Allogene based on an exclusive license granted by Cellectis to Servier. ALLO-501 uses Cellectis technologies. Servier grants to Allogene exclusive rights to ALLO-501 in the U.S. while Servier retains exclusive rights for all other countries.