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# POSTER ABSTRACTS

## 704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

### ALLO-647 for Lymphodepletion in the Allogeneic CAR T Setting: Safety Experience with ALLO-501/501A in Patients (Pts) with Relapsed/Refractory (r/r) Large B-Cell and Follicular Lymphomas

*Frederick L. Locke, MD*[1], *Javier L. Munoz*[2], *Michael T. Tees, MD*[3], *Lazaros J. Lekakis*[4], *Herbert A. Eradat, MD*[5], *Sven de Vos, MD PhD*[5], *Rajneesh Nath*[6], *Don A. Stevens*[7], *Shahbaz A. Malik, MD*[8], *Geoffrey P. Shouse, PhDDO*[9], *Mehdi Hamadani, MD*[10], *Olalekan O. Oluwole, MBBS*[11], *Miguel-Angel Perales, MD*[12], *David B. Miklos, MD PhD*[13], *Anh Nguyen*[14], *Amy Feng*[14], *Lynn Navale*[14], *Elaine Murray*[14], *Greg P. Kaufman*[14], *Kazuharu Kai*[14], *John B. Le Gall*[14], *Sattva S. Neelapu, MD*[15]

[1] H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL
[2] Mayo Clinic, Scottsdale, AZ
[3] The Colorado Blood Cancer Institute a part of Sarah Cannon Cancer Institute at Presbyterian/St Luke's Medical Center, Denver, CO
[4] University of Miami, Miami, FL
[5] Department of Medicine/Division of Hematology and Oncology, UCLA Medical Center, Los Angeles, CA
[6] Banner MD Anderson Cancer Center, Scottsdale, AZ
[7] Norton Cancer Institute, Louisville, KY
[8] St. David's South Austin Medical Center, Austin, TX
[9] Hematology/HCT, City of Hope National Medical Center, Duarte, CA
[10] Division of Hematology and Oncology, The Medical College of Wisconsin Inc, Milwaukee, WI
[11] Division of Hematology/Oncology, Vanderbilt University Medical Center, Nashville, TN
[12] Adult Bone Marrow Transplantation Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY
[13] Division of Blood and Marrow Transplantation & Cellular Therapy, Stanford University, Palo Alto, CA
[14] Allogene Therapeutics, San Francisco, CA
[15] Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX

**Background:** While breakthroughs in hematologic malignancies with autologous CAR T-cell therapies have been met with growing clinical interest due to impressive outcomes, limitations in logistics/manufacturing, quality consistency, and product availability persist. Allogeneic CAR T-cell therapies may circumvent such challenges by providing an off-the-shelf therapeutic option derived from healthy donors.

For allogeneic CAR T cells to be successful, there must be a safe and effective way to control host lymphocyte rejection of allogeneic CAR T cells (allo-rejection). ALLO-501 and ALLO-501A are allogeneic anti-CD19 CAR T-cell products that use Cellectis technologies' TALEN® gene editing to disrupt both the TCR*α* constant ( *TRAC*) and CD52 genes. CD52 disruption specifically permits use of ALLO-647, an anti-CD52 antibody, for the transient and selective depletion of host lymphocytes that enables ALLO-501 and ALLO-501A to proliferate after infusion without rapid allo-rejection.

Updated phase 1 data for ALLO-501 (ALPHA; NCT03939026) and ALLO-501A (ALPHA2; NCT04416984) showed that administration of anti-CD19 allogeneic CAR T product following use of lymphodepletion that includes ALLO-647 plus fludarabine and cyclophosphamide provided durable responses and an acceptable safety profile in CAR T-cell-naive pts with r/r large B-cell lymphoma (LBCL; Locke FL, et al. ASCO 2023; #2517). Herein, we provide safety results of ALLO-647 in pts with r/r LBCL and follicular lymphoma (FL).

**Methods:** Pts with r/r LBCL and FL enrolled in ALPHA and ALPHA2 studies received a 3 to 5-day lymphodepletion regimen consisting of fludarabine 30 mg/m $^2$ and cyclophosphamide 300-500 mg/m $^2$ (FC) and 39, 60, or 90 mg of ALLO-647 in divided doses. ALLO-501/ALLO-501A were administered after the completion of lymphodepletion. Incidence rates of grade ≥3 cytopenias (neutropenia, thrombocytopenia, anemia and pancytopenia) were assessed at 3 timepoints (Study Day 28, Day 56, and Month 4). Pts underwent weekly cytomegalovirus (CMV) monitoring. Leukocyte reconstitution was evaluated following lymphodepletion and CAR T-cell infusion.

**Results:** As of April 20, 2023, 87 pts with r/r LBCL (n=61) and FL (n=26) were treated with ALLO-647 and included in the analysis (median age, 64 years; median number of prior regimens, 3). In total, 11 (13%), 39 (45%), and 37 (43%) pts received 39, 60, and 90 mg ALLO-647, respectively. Among the LBCL pts, 33 were CAR T-cell-naive and treated with product manufactured using the Phase 2 process. Median follow-up was 29.5 months (range, 6.8-47.5).

The most common treatment-emergent adverse events (TEAEs), assessed from the time of first dose of lymphodepletion, included neutropenia (79%), anemia (61%), infusion-related reactions (IRRs, 55%), and thrombocytopenia (53%). The most common grade ≥3 TEAEs included neutropenia (74%), anemia (38%), and thrombocytopenia (38%). The proportion of pts experiencing grade ≥3 cytopenias decreased over time from Day 28 (29%) to Day 56 (20%) to Month 4 (15%), which was consistent across all lymphoma pt subgroups.

ALLO-647 IRRs were typically low grade, except for 5 (6%) grade 3 events; all IRRs were managed with supportive care measures. After treatment with ALLO-501/501A, 20 pts (23%) experienced cytokine release syndrome events, which were low grade except for 1 (1%) grade 3 event. No GvHD, grade ≥3 immune effector cell-associated neurotoxicity syndrome events, or progressive multifocal leukoencephalopathy were reported.

Any grade and grade ≥3 infections were reported in 50 pts (58%) and 18 pts (21%), respectively. Two pts had (2%) fatal infectious events (COVID-19 pneumonia and pneumonia, n=1 each) as previously reported. The most common infection was CMV reactivation (any grade, n=22 [25%]; grade 3, n=8 [9%]).

Following lymphodepletion, the median time to absolute neutrophil count and absolute lymphocyte count recovery to grade <4 was 7 days and 28 days, respectively. T-cell counts exhibited a steady increase over time, with the majority of pts achieving full T-cell recovery (return to baseline levels) by Month 6. Detailed pharmacokinetics and pharmacodynamics data will be presented.

**Conclusions:** These data suggest allogeneic CAR T-cell products administered following lymphodepletion consisting of FC and ALLO-647 can provide a safe and tolerable alternative to autologous CAR T-cell therapy.

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