First-Line Consolidation With Cemacabtagene Ansegedleucel (Cema-Cel) in Patients With Large B-Cell Lymphoma and Minimal Residual Disease After Response to Standard Therapy: The Pivotal, Randomized, Open-Label Phase 2 ALPHA3 Study

Poster 3730

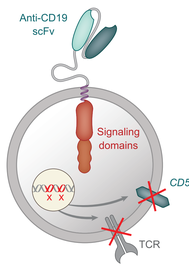
John M. Burke,[1] Nancy L. Bartlett,[2] Gary L. Simmons,[3] Lindsey A. Fitzgerald,[4] Jeremy S. Abramson,[5] Akil A. Merchant,[6] Paolo F. Caimi,[7] Rushang D. Patel,[8] Don A. Stevens,[9] Sven de Vos,[10] Oleg L. Krijanovski,[11] Geoffrey Shouse,[12] Alex F. Herrera,[12] Houston Holmes,[13] Matthew Matasar,[14] Mitul Gandhi,[15] Frederick L. Locke,[16] John Kuruvilla,[17] Amy Feng,[18] Joe Jiang,[18] Shilpa Shahani,[18] John B. Le Gall,[18] Zachary J. Roberts,[18] Jason Westin,[19] on behalf of the ALPHA3 investigators

[1]Sarah Cannon Research Institute, Rocky Mountain Cancer Centers, Nashville, TN, USA; [2]Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, USA; [3]Virginia Oncology Associates, Norfolk, VA, USA; [4]Huntsman Cancer Institute/University of Utah, Salt Lake City, UT, USA; [5]Center for Lymphoma, Massachusetts General Hospital Cancer Center, Boston, MA, USA; [6]Cedars-Sinai Medical Center, Los Angeles, CA, USA; [7]Case Western Reserve and Cleveland Clinic, Cleveland, OH, USA; [8]Stem Cell Transplant and Cellular Therapy, AdventHealth, Orlando, FL, USA; [9]Norton Cancer Institute, Louisville, KY, USA; [10]UCLA Santa Monica Medical Center, Santa Monica, CA, USA; [11]Alta Bates Summit Medical Center Comprehensive Cancer Center, Berkeley, CA, USA; [12]City of Hope National Medical Center, Duarte, CA, USA; [13]Texas Oncology/Baylor Sammons Cancer Center, Dallas, TX, USA; [14]Rutgers Cancer Institute, New Brunswick, NJ, USA; [15]Virginia Cancer Specialists, Gainesville, VA, USA; [16]Moffitt Cancer Center, Tampa, FL, USA; [17]Princess Margaret Cancer Centre, Toronto, ON, Canada; [18]Allogene Therapeutics, San Francisco, CA, USA; [19]The University of Texas MD Anderson Cancer Center, Houston, TX, USA

BACKGROUND

- Standard first-line (1L) therapy for large B-cell lymphoma (LBCL) has a cure rate of approximately 60%; however, approximately 30% of responders relapse within 2 years[1-3]
- Identifying patients at high risk of relapse after achieving a response to 1L therapy allows for remission consolidation, potentially increasing 1L cure rates and changing the current lymphoma treatment paradigm
  - Presence of circulating tumor DNA (ctDNA)–based minimal residual disease (MRD), measured by an ultrasensitive MRD test at the end of 1L therapy, is highly prognostic for relapse[4]
- Cemacabtagene ansegedleucel (cema-cel), an immediately available, off-the-shelf, human leukocyte antigen-unmatched allogeneic CD19 chimeric antigen receptor (CAR) T-cell product (**Figure 1**), is a promising agent for consolidation in this treatment setting
- Cema-cel has shown potent antitumor activity and manageable safety in phase 1 studies of patients with relapsed/refractory LBCL[5,6]
- Consolidating remission of LBCL in patients at high risk of recurrence ensures treatment prior to aggressive relapse or development of new comorbidities that could preclude treatment in later lines. Additionally, treatment in the low disease burden state may cause fewer treatment-related toxicities[7-9]
- Here, we report the updated design of the pivotal randomized, open-label, phase 2 ALPHA3 study, which is evaluating the efficacy and safety of consolidation with cema-cel compared with standard-of-care (SOC) observation in patients with LBCL who are in response after 1L immunochemotherapy but have detectable MRD by ctDNA-based testing

Figure 1. Cemacabtagene Ansegedleucel (Cema-Cel)[a]



CAR, chimeric antigen receptor; scFv, single-chain fragment variable; TCR, T-cell receptor.
[a]Utilizes Cellectis technologies.
[b]This would enable use of ALLO-647, but ALLO-647 is no longer part of the ALPHA3 study.

METHODS

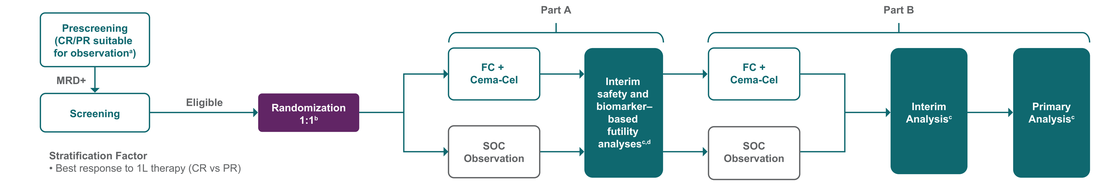
- ALPHA3 (NCT06500273) consists of a 2-part seamless design (**Figure 2**)
  - Part A
    - Patients will be randomly assigned 1:1 to SOC observation or to cema-cel (120×10^6 CAR T cells) after a 3-day lymphodepletion (LD) with fludarabine (30 mg/m^2/day) and cyclophosphamide (300 mg/m^2/day) (FC)
    - Patients enrolled in Part A will be included in the inferential testing in Part B
  - Part B
    - Patients will continue to be randomly assigned 1:1 to cema-cel after FC LD or SOC observation
- All treatments can be administered in the outpatient setting
- Study endpoints are listed in **Table 1**
- To be eligible to screen for the ALPHA3 study, patients must successfully complete prescreening (**Figure 3**; **Table 2**)
  - Posttreatment positron emission tomography/computed tomography (PET/CT) must show complete response or partial response for which the SOC would be close observation (eg, negative biopsy of PET-avid lesion)
  - ctDNA-based MRD testing requires a tumor sample from initial diagnosis and a blood sample collected at or shortly after end-of-treatment PET/CT scan

Table 1. Study Endpoints

Primary
• EFS per IRC[a,b]
Secondary
• PFS per IRC[a,b]
• OS[b]
• Rate of MRD clearance
• EFS per investigator[a]
• PFS per investigator[a]
• Safety
Exploratory
• PK/PD (cema-cel)
• Immunogenicity
• PROs

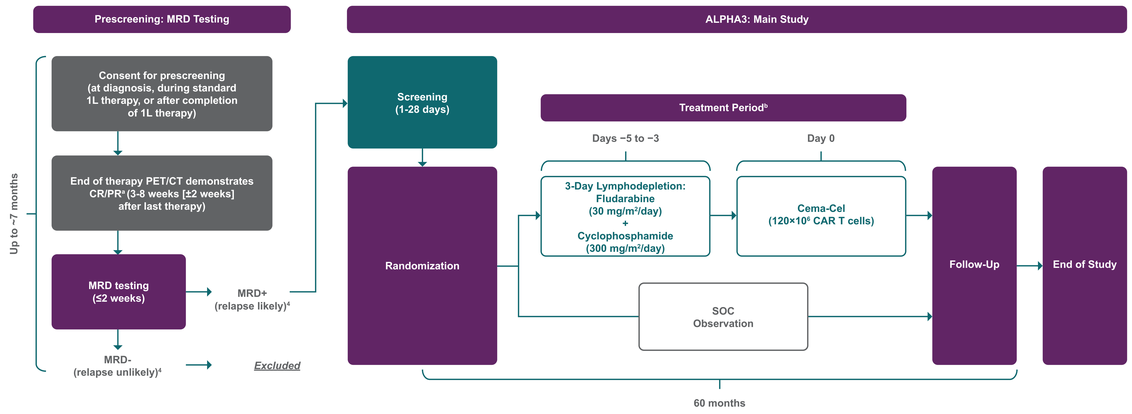
cema-cel, cemacabtagene ansegedleucel; EFS, event-free survival; IRC; independent review committee; MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival; PK/PD, pharmacokinetics/pharmacodynamics; PRO, patient-reported outcome.
[a]Assessed per Lugano 2014 criteria.
[b]EFS per IRC, PFS per IRC, and OS will undergo hierarchical testing.

Figure 2. ALPHA3 Study Design



1L, first line; cema-cel, cemacabtagene ansegedleucel; CR, complete response; EFS, event-free survival; FC, fludarabine (30 mg/m^2/day) and cyclophosphamide (300 mg/m^2/day); IRC, independent review committee; LD, lymphodepletion; MRD, minimal residual disease; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; PK/PD, pharmacokinetics; PR, partial response; PRO, patient-reported outcome; SOC, standard of care.
Approximately 250 participants will be randomly assigned to treatment with cema-cel or SOC observation.
[a]PR suitable for observation is defined as intent to observe the patient without further treatment (including radiation therapy) until definitive disease progression.
[b]A second cema-cel arm that utilized 3-day LD with FC plus the anti-CD52 monoclonal antibody ALLO-647 (30 mg/day) was closed in August 2025.
[c]Patients enrolled in Part A will be included in the inferential testing in Part B.
[d]The interim safety- and surrogate biomarker–based futility analyses will occur when 12 patients are randomly assigned and followed for 45 days in each treatment arm.

Figure 3. ALPHA3 Study Patient Journey



1L, first line; CAR, chimeric antigen receptor; cema-cel, cemacabtagene ansegedleucel; CR, complete response; CT, computed tomography; MRD, minimal residual disease; PET, positron emission tomography; PR, partial response; SOC, standard of care.
[a]PR suitable for observation is defined as intent to observe the patient without further treatment (including radiation therapy) until definitive disease progression.
[b]All treatments can be administered in the outpatient setting.

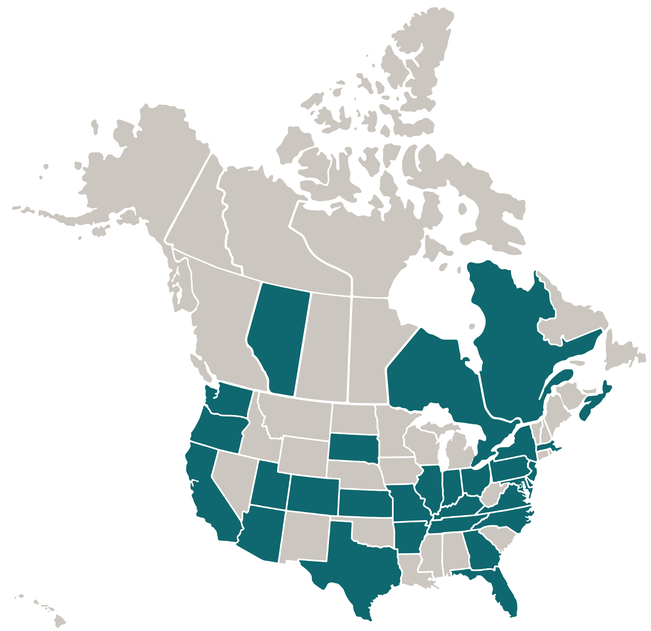
Table 2. Key Study Eligibility Criteria

Prescreening	Main Study Screening	
Criteria for MRD Testing	**Key Inclusion Criteria**	**Key Exclusion Criteria**
Histologically confirmed diagnosis of DLBCL,[a] HGBCL, or PMBCL and at least 1 of the following clinical criteria: IPI score of 2-5 at diagnosis, Ann Arbor stage III or IV disease at diagnosis, equivocal response at interim or EOT PET/CT	MRD+ by ctDNA-based testing	Prior treatment with CD19-targeted therapies
Completed a full course of standard 1L therapy (must have included an anthracycline and an anti-CD20 monoclonal antibody); for example: • R-CHOP • Pola-R-CHP • DA-EPOCH-R	ECOG PS of 0 or 1	History of CNS involvement, transformation from other malignancy (transformed FL or MZL, or Richter transformation), or T-cell/histiocyte-rich LBCL
Achieved a CR or PR suitable for observation[b] at the completion of 1L treatment based on PET/CT evaluation per Lugano 2014 criteria	No progression since MRD testing; response on PET/CT within 5 weeks prior to randomization	History of clinically significant CNS dysfunction (eg, seizure disorder [uncontrolled in last 12 months], cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, cerebral edema)
MRD samples available for submission • Adequate tumor specimen from initial diagnosis • Adequate blood sample collected after final 1L treatment	Adequate hematologic, cardiac, pulmonary, renal, and hepatic function	Treatment with systemic immunosuppressive agents within 2 weeks or 5 half-lives (whichever is shorter) prior to enrollment[c]

1L, first line; CNS, central nervous system; CR, complete response; CT, computed tomography; DA-EPOCH-R, dose-adjusted rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end of therapy; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; IPI, International Prognostic Index; LBCL, large B-cell lymphoma; MRD, minimal residual disease; MZL, marginal zone lymphoma; PET, positron emission tomography; PMBCL, primary mediastinal B-cell lymphoma; pola-R-CHP, polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin, and prednisone; PR, partial response; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.
[a]Includes DLBCL not otherwise specified, Epstein-Barr virus+ DLBCL, DLBCL with *IRF4/MUM1* rearrangement, high-grade B-cell lymphoma, and primary mediastinal B-cell lymphoma.
[b]PR suitable for observation is defined as intent to observe the patient without further treatment (including radiation therapy) until definitive disease progression.
[c]Corticosteroids for physiologic replacement (<10 mg/day of prednisone equivalents) is acceptable.

STUDY STATUS AND CONTACTS

- Patients are being enrolled across academic- and community-based centers in the United States and Canada
- For more information, please visit www.clinicaltrials.gov
- Contact email: ALPHA3@allogene.com



Active Study Locations

Canada	United States			
Alberta	Arizona	Illinois	New Jersey	Tennessee
Nova Scotia	Arkansas	Indiana	New York	Texas
Ontario	California	Kansas	North Carolina	Utah
Quebec	Colorado	Kentucky	Ohio	Virginia
	Delaware	Maryland	Oregon	Washington
	Florida	Massachusetts	Pennsylvania	Washington, DC
	Georgia	Missouri	South Dakota	

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Allogene's investigational AlloCAR T™ oncology products utilize Cellectis technologies. These products are developed based on an exclusive license granted by Cellectis to Servier. Servier, which has an exclusive license to the anti-CD19 AlloCAR T™ investigational products from Cellectis, has granted Allogene exclusive rights to these products in the U.S., all EU Member States, and the United Kingdom. Medical writing and/or editorial assistance was provided by Obinna T. Ezeokoli, PhD, and Robert Steger, PhD, of ApotheCom (Yardley, PA, USA). This assistance was funded by Allogene Therapeutics, Inc.

CONTACT INFORMATION

Contact the author at john.burke@uoncology.com for questions or comments.

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