ALPHA3 Clinical Trial is Now Enrolling!

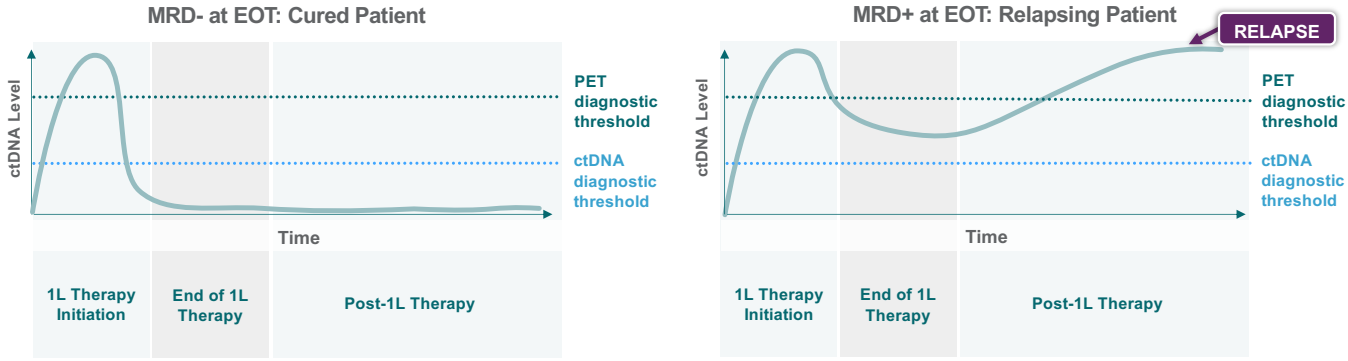
ALPHA3: Study Rationale

The ALPHA3 trial is aiming to transform the standard of care for patients with newly diagnosed LBCL. Today, for patients in remission after first-line. (1L) therapy, we watch and wait to see if the patient relapses. In ALPHA3, we aim to identify the patients most at risk of relapse through a highly sensitive investigational ctDNA-based MRD test; and, for those patients with MRD, to prevent relapse with an off-the-shelf CAR T therapy, cemacabtagene ansegedleucel (cema-cel).

ctDNA-Based MRD Assessment in LBCL May Predict Cure or Relapse Better than PET/CT

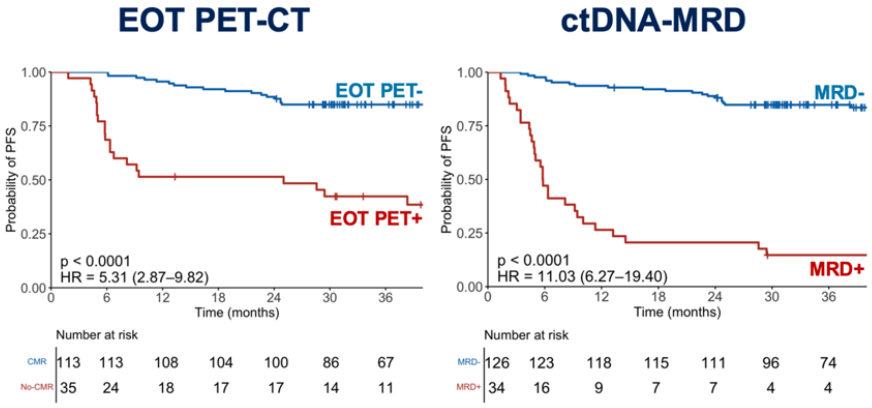
MRD detection by ctDNA is a promising method for early relapse prediction in LBCL, improving detection of residual disease at the end of 1L therapy over PET/CT imaging[1-5]

ctDNA following 1L therapy is associated with high rates of clinical relapse and poor EFS and OS[2-4]



1. Roschewski M, et al. Hematol Oncol. 2023;41(suppl 2):177-179. 2. Kurtz DM, et al. J Clin Oncol. 2018;36(28):2845-2853. 3. Roschewski M, et al. Lancet Oncol. 2015;16(5):541-549. 4. Herrera AF, et al. Blood Adv. 2022;6(6):1651-1660. 5. Macaulay C, et al. Am J Hematol. 2019;134(suppl 1):1600.

Foresight CLARITY™ IUO MRD test leverages PhasED-Seq technology for ctDNA-based MRD detection, potentially offering a highly sensitive and prognostic indicator of relapse in LBCL that has shown association with clinical outcomes in prior studies[1]



In a prospective, multi-center validation study in 1L DLBCL patients, end of therapy landmark MRD detection by Foresight CLARITY™ more strongly stratified relapse risk vs. PET/CT-demonstrating >80% clinical sensitivity to predict relapse within one year of 1L therapy.

Wang, et al. ASCO 2025

1L, first line; CNS, central nervous system; ctDNA, circulating tumor DNA; DLBCL, diffuse large B-cell lymphoma; EFS, event-free survival; EOT, end of therapy; LBCL, large B-cell lymphoma; MRD, minimal residual disease; OS, overall survival; PET/CT, positron emission tomography/computed tomography; PFS, progression free survival.

Allogene® THERAPEUTICS

ALPHA3: Key Study Details

ALPHA3 is the first randomized, open-label, multicenter, phase 2 study evaluating the efficacy and safety of a one-time allogeneic CAR T product versus standard-of-care observation in participants with LBCL who are in response at the completion of 1L therapy and potentially at high risk of relapse based on an investigational ctDNA-based MRD testing method using PhasED-Seq technology.

Safety and efficacy of cema-cel in relapsed or refractory DLBCL in ALPHA and ALPHA2 studies are encouraging and support potentially improving outcomes in the front-line setting

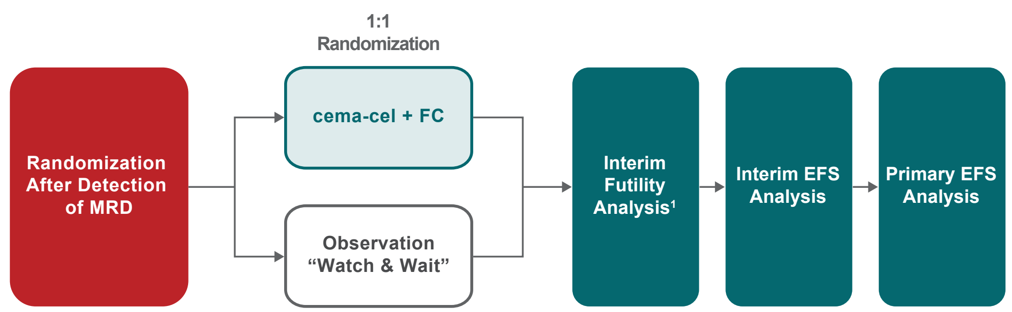
	Median Time From Enrollment to Treatment = 2 days				
3L Relapsed/Refractory LBCL	**All Patients (n=33)**	**Patients Who Received Selected Ph2 Dose* (n=12)**	**KYMRIAH®[1]** Phase 2 Pivotal	**YESCARTA®[2]** Phase 2 Pivotal	**BREYANZI®[3]** Phase 2 Pivotal
ORR	58%	67%	50% (label)	72% (label)	73% (label)
CR in LBCL (mITT)	42%	58%	32% (label)	51% (label)	54% (label)
CR at 6 months in LBCL (mITT)	30%	42%	29%	36%	~ 40%
DOR (months)	11.1	23.1	NE (label)	9.2 (label)	16.7 (label)
CRS (Gr3+)	0%	0%	22%	13%	4%
Neuro Events (Gr3+)	9%	0%	12%	31%	12%
Infection (Gr3+)	15%	8%	20%	23%	19%
Enrolled who did not receive intended cell product	n=3	n=1***	33%**	9%**	36%^

[1] KYMRIAH USPI and Schuster S et al NEJM 2019. Patient population in the label includes: 78% - primary DLBCL not otherwise specified (NOS); 22% DLBCL following transformation from Follicular Lymphoma
[2] YESCARTA USPI and Neelapu, NEJM 2017. Patient population in the label includes: 76% - DLBC; 16% - Transformed Follicular Lymphoma; 8% Primary Mediastinal Large B-cell Lymphoma.
[3] BREYANZI USPI and Abramson, Lancet, 2020. Patient population in label includes: 53% - de novo DLBCL; 25% DLBCL transformed from indolent Lymphoma; 14% high-grade B-cell Lymphoma; 7% Primary Mediastinal Large B-cell Lymphoma; 1% grade 3B Follicular Lymphoma
*Fludarabine/cyclophosphamide lymphodepletion with 90 mg of ALLO-647 (FCA90) followed by a single dose of CAR T cells at 120 x 106 494 CAR+ cells
**Percent of patients who enrolled and did not receive intended cell product including out of spec products
***After enrollment, one subject was found to have CNS involvement and was excluded
^Percent who underwent lymphodepletion but did not receive intended cell product including out of spec products
FOR ILLUSTRATIVE PURPOSES ONLY: no head-to-head clinical trial has been conducted. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.
ALPHA/ALPHA2 Data Cutoff Date: April 20, 2023, ICML 2023

Cema-cel is an off-the-shelf, allogeneic CD19 CAR T product candidate that has shown promise in the phase 1 trial ALPHA2 (NCT04416984) and, together with additional Phase 1 data from an allogeneic CAR T predecessor to cema-cel studied in the ALPHA (NCT03939026) trial, form the rationale for treating patients with treatment-resistant LBCL. In ALPHA and ALPHA2, participants with relapsed or refractory LBCL after a median of 3 lines of therapy achieved a 67% ORR and 58% CR rate, and the rate of cytokine release syndrome (CRS) was 33%, with no grade 3+ CRS and no ICANS.[1]

This encouraging anti-disease activity and outpatient-friendly safety profile in patients with gross, relapsed/refractory disease may improve in patients with MRD only disease when they are treated after a single line of therapy. Cema-cel's off-the-shelf availability as a one-time treatment administered shortly after completion of 1L care in patients likely to relapse may improve cure rates without the uncertainty associated with current relapse and salvage therapies.

ALPHA3 Study Design



FC: Fludarabine 30 mg/m2/day, Cyclophosphamide 300 mg/m2/day, administered daily x 3 days. Cema-cel: 120 million CAR+ cells.

[1] Futility analyses will occur with minimum 12 patients enrolled in each arm
[2] Assessed per Lugano 2014 criteria.
[3] EFS per IRC, PFS per IRC, and OS underwent hierarchical testing.

Primary Endpoint
EFS per Blinded IRC assessment[2]

Secondary Endpoints
PFS per IRC assessment[2,3]

OS

Rate of conversion to MRD-

Eligible participants with MRD will be randomized to treatment or observation arms. Treatment will consist of a one-time infusion of cema-cel after a 3-day lymphodepletion regimen. Participants who are randomized to the observation arm will be closely monitored (initially every 3 months for the first year) to enable prompt detection and action in case of disease relapse.

ALPHA3: Study Status

ALPHA3 is actively recruiting patients with approximately 240 patients to be enrolled at both academic and community-based centers.

Further information about this study, including study centers, can be found here:

bitly

Updated August 2025