ALPHA3 Clinical Trial is Now Enrolling!

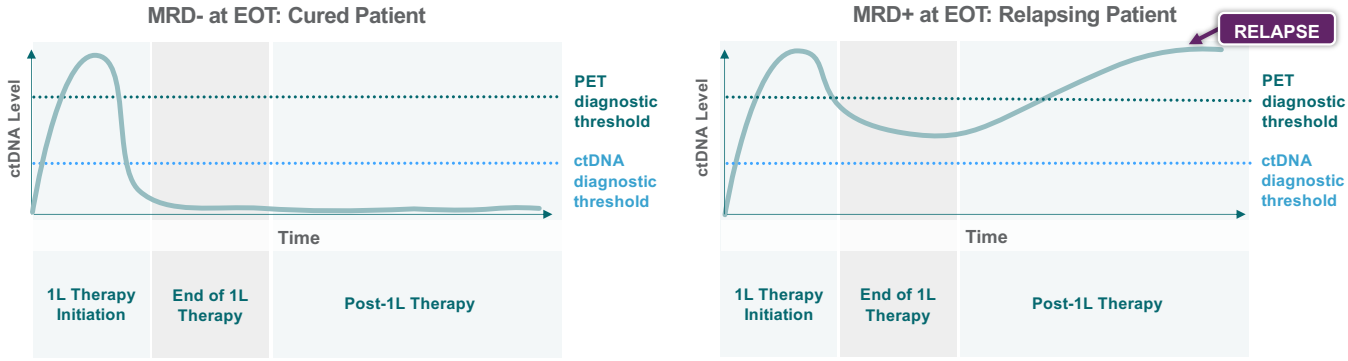
ALPHA3: Study Rationale

The ALPHA3 trial is aiming to transform the standard of care for patients with newly diagnosed LBCL. Today, for patients in remission after frontline (1L) therapy, we watch and wait for relapse. 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

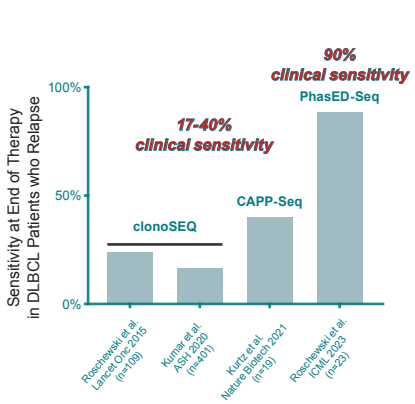
MRD detection by ctDNA is a promising method for early relapse prediction in LBCL, improving detection of residual disease at the end of 1L therapy over PET/CT imaging[1-5]

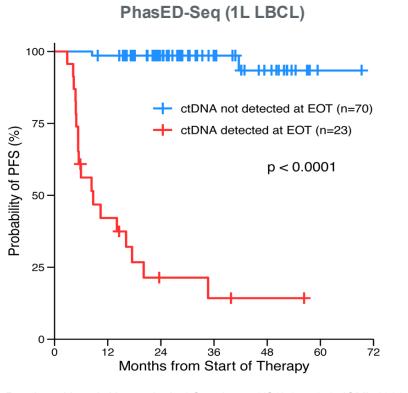
ctDNA following 1L therapy is associated with high rates of clinical relapse and poor EFS and OS[2-4]



The Foresight CLARITY™ IUO MRD Test Is Currently Only Available in ALPHA3

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]





Roschewski et al. *Hematological Oncology* 41(S2):177-179, ICML 2023

In a pooled analysis of 5 prospective 1L DLBCL cohorts, end of therapy landmark PhasED-Seq accurately stratified patients:

- Among patients (n=23) who are MRD+, ~90% had progression events within 36 months
- Among patients (n=70) who are MRD-, only 2 had PFS events of CNS recurrence and death from non lymphoma

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.

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.

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.

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 24%, with no grade 3+ CRS and no ICANS.[1]

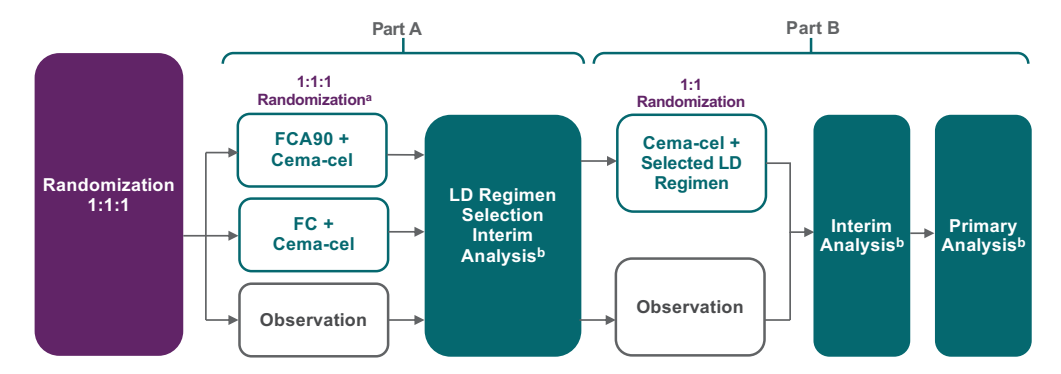
Safety and efficacy of cema-cel in relapsed or refractory DLBCL in ALPHA and ALPHA2 studies are encouraging and support potentially improving outcomes in the front-line setting

	All Alloy (n=33)	FCA90 Alloy (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%
CRS (Gr3+)	0%	0%	22%	13%	4%
Neuro Events (Gr3+)	6%	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
**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

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



Primary Endpoint

- EFS per IRC assessment[c]

Secondary Endpoints

- PFS per IRC assessment[c,d]
- Overall survival[d]
- Rate of MRD clearance
- EFS and PFS per investigator[c]
- Safety (cema-cel and ALLO-647)

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

The ALPHA3 study is actively recruiting and is anticipated to open in approximately 50 academic and community-based cancer centers with expected enrollment of approximately 240 patients.

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

a Randomization ratio may be adjusted after the safety interim analysis.

b Safety and interim efficacy analyses will occur and culminate in LD regimen selection. Patients treated with the selected regimen or followed in observation during Part A will be included in inferential testing in Part B.

c Assessed per Lugano 2014 criteria. d EFS per IRC, PFS per IRC, and OS underwent hierarchical testing.

Cema cel, cemacabtagene ansegedleucel; EFS, event free survival; FC, fludarabine and cyclophosphamide; FCA90, fludarabine and cyclophosphamide and ALLO 647 (90 mg); IRC, independent review committee; LD, lymphodepletion, MRD, minimal residual disease; OS, overall survival; PFS, progression free survival; PR, partial response.

1. Locke FL, et al. ICML 2023. Hematol Oncol. 2023;41(suppl 2):85-86.