# Study of LYL314 in Aggressive Large B-Cell Lymphoma

**Status:** RECRUITING

## Eligibility Criteria

**Age:** 18 years and over

This study is NOT accepting healthy

**Healthy Volunteers:** volunteers

**Inclusion Criteria:**

1. Age 18 years or older at time of informed consent 2. Willing and able to provide written informed consent 3. Histologically confirmed aggressive NHL, including the following types defined by the World Health Organization (WHO 2017): * DLBCL * DLBCL arising from follicular lymphoma (transformed FL, tFL) * Primary mediastinal (thymic) large B-cell lymphoma (PMBCL) * High-grade large B-cell lymphoma with or without MYC and BCL2 and/or BCL6 rearrangement (HGBL) * Grade 3B follicular lymphoma/Large cell follicular lymphoma (FL3B) 4. Received at least two prior lines of therapy for Cohorts 1, 2, and 4 and one prior line of therapy for Cohort 3. Prior therapy must have included: * Anti-CD20 monoclonal antibody, and * An anthracycline containing chemotherapy regimen * Participants with tFL must have received at least one of their prior lines of therapy after transformation to DLBCL 4b. Cohort 5 (High-risk first-line) participants must have high-risk large B-cell lymphoma 5. Relapsed or refractory disease, defined by the following: * Disease progression after last regimen (including salvage therapy after autologous stem cell transplantation \[ASCT\]). In participants who have only received front-line therapy, progression should be ≤ 12 months of first-line therapy (applicable for Cohort 3) * In patients who received one line of therapy, refractory disease is defined as failure to achieve at least a PR after at least 4 cycles of therapy (applicable for Cohort 3) * In patients who received two or more lines of therapy (Cohorts 1, 2, and 4), refractory disease is defined as failure to achieve a CR to last line of therapy (including CAR T and/or salvage therapy). 6. At least 1 measurable lesion (per Lugano classification). Lesions that have been previously irradiated will be considered measurable only if progression has been documented following completion of radiation therapy 7. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 or ECOG 0 to 2 (Cohort 5) 8. Absolute neutrophil count (ANC) ≥ 1000/uL 9. Platelet count ≥ 50,000/uL 10. Absolute lymphocyte count (ALC) ≥ 200/uL Other protocol-defined criteria apply.

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**Exclusion Criteria:**

1. History of malignancy other than non-melanoma skin cancer or carcinoma in situ (e.g., cervix, bladder, breast) unless disease-free for at least 3 years. Participants who have received therapy for a prior malignancy within the prior 3 years, e.g., in the adjuvant setting, are not excluded 2. Active central nervous system (CNS) involvement by malignancy on magnetic resonance imaging (MRI) or by lumbar puncture. Participants with prior evidence of brain metastasis treated at least 8 weeks prior to enrollment will not be excluded for participation if CNS disease is deemed stable at the time of study enrollment 3. History of cardiac lymphoma involvement or Epstein-Barr virus (EBV)+ lymphoma 4. Ongoing or impending oncologic emergency (e.g., tumor mass effect, tumor lysis syndrome, known vascular invasion) 5. Received the following therapies in the specified time frame prior to enrollment/leukapheresis 1. Any systemic therapy within 2 weeks 2. Any systemic inhibitory/stimulatory immune checkpoint molecule therapy within 3 half-lives prior to enrollment (e.g., ipilimumab, nivolumab, pembrolizumab, atezolizumab, OX40 agonists, 4-1BB agonists) 3. Fludarabine within 12 weeks 4. Alemtuzumab, bendamustine or antithymocyte globuline (ATG) within 6 months 5. Any T cell engager/bispecific antibody therapy such as CD20/CD3 or CD19/CD3 bispecific antibodies within 4 weeks 6. Any experimental therapy within 4 weeks or 5 half-lives (whichever is shorter) 6. Received radiation therapy within 3 weeks prior to enrollment/leukapheresis 7. Experiencing non-hematologic toxicities due to prior therapy. Exceptions include: stable and recovered to grade ≤ 1 or non-clinically significant toxicities such as (1) alopecia, (2) toxicities where Grade 2 is solely defined by participant receiving hormone replacement therapy for endocrinopathies resulting from previous checkpoint inhibitor therapy, (3) Grade 2 lymphopenia, and (4) hearing loss or Grade 2 neuropathy associated with prior treatment with taxanes or platinating agents 8. History of allogeneic stem cell or solid organ transplantation 9. Receipt of autologous stem cell transplantation within 6 weeks prior to enrollment/leukapheresis 10. History of prior genetically modified cell therapy other than a product targeting CD19 with an FMC63-based CAR (e.g., axicabtagene ciloleucel (axi-cel), tisagenlecleucel (tisa-cel), or lisocabtagene maraleucel (liso-cel). For all other CAR T cell therapy treatments, discussion with the Sponsor's Medical Monitor is required 11. Primary immunodeficiency 12. History of autoimmune disease (e.g., Crohn's disease, rheumatoid arthritis, systemic lupus) resulting in end organ injury or requiring systemic immunosuppression/systemic disease modifying agents within the last 2 years. Participants who have other autoimmune condition(s) considered to be associated with underlying malignancy may be enrolled in the study after discussion with and approval of the Medical Monitor. Other protocol-defined criteria apply.

## Conditions & Interventions

**Interventions:**
DRUG: LYL314, DRUG: Fludarabine, DRUG: Cyclophosphamide
**Conditions:**
Relapsed Non-Hodgkin Lymphoma, Refractory Non-Hodgkin Lymphoma, Non-Hodgkin Lymphoma, Large B-cell Lymphoma
**Keywords:**
CAR T-cell, Non-Hodgkin Lymphoma, CD19/20, CD19, CD20, NHL, Diffuse Large B-cell lymphoma, DLBCL, Transformed follicular lymphoma, TFL, Primary mediastinal B-cell lymphoma, PMBCL, High-grade B-cell lymphoma, HGBL, follicular lymphoma Grade 3B, large cell follicular lymphoma, Aggressive B-cell NHL, Refractory Aggressive B-Cell Lymphoma, Refractory B-Cell Non-Hodgkin Lymphoma, Lymphoma, Non-Hodgkin, Lymphoma, Lymphoma, Large B-Cell, Diffuse, Cyclophosphamide, Fludarabine, Lymphoma, Follicular, Lymphoma, B-cell, Immunosuppressive Agents, Immunologic Factors, Disease Attributes, Immune System Diseases, Recurrence, PiNACLE

## More Information

**Contact(s):** Lyell Immunopharma Inc. - clinicaltrials@lyell.com
**Principal Investigator:**
**Phase:** PHASE1
**IRB**
**Number:**
**System ID:** NCT05826535

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