

4.2. Inclusion Criteria

Subjects must satisfy the following criteria to be enrolled in the study:

1. Subject is ≥ 18 years of age at the time of signing the informed consent form (ICF).
2. Subject must understand and voluntarily sign an ICF prior to any study-related assessments/procedures being conducted.
3. Subject is willing and able to adhere to the study visit schedule and other protocol requirements.
4. Investigator considers the subject is appropriate for adoptive T cell therapy.
5. Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2.
6. Subjects with one of the following:
 - Cohort 1: Subjects with DLBCL NOS (de novo or tFL), high-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements with DLBCL histology (DHL/THL) and FL3B per WHO 2016 classification ([Swerdlow, 2016](#)), after ≥ 2 lines of therapy, including an anthracycline and rituximab (or other CD20-targeted agent).
7. Histological confirmation of diagnosis at last relapse. Enough tumor material must be available for central confirmation of diagnosis, otherwise a new tumor biopsy is mandated. NOTE: if subsequent therapies are given after last relapse with SD/PD as best response, the tissue from that last relapse will be considered adequate to participate in the
10. Adequate organ function, defined as:
 - Adequate bone marrow function to receive LD chemotherapy as assessed by the Investigator.
 - Serum creatinine $< 1.5 \times$ age-adjusted upper limit of normal (ULN) or creatinine clearance > 30 mL/min (estimated glomerular filtration rate [eGFR] by Cockcroft-Gault).
 - Alanine aminotransferase (ALT) \times ULN and total bilirubin < 2.0 mg/dL (or < 3.0 mg/dL for subjects with Gilbert's syndrome or lymphomatous infiltration of the liver).
 - Adequate pulmonary function, defined as \leq Grade 1 dyspnea according to Common Toxicity Criteria for Adverse Events (CTCAE) and SaO₂ $\geq 92\%$ on room air.
 - Adequate cardiac function, defined as left ventricular ejection fraction (LVEF) $\geq 40\%$ as assessed by echocardiogram or multigated acquisition (MUGA) scan performed within 4 weeks prior to leukapheresis.
11. Adequate vascular access for leukapheresis procedure.
12. Subjects must agree to not donate blood, organs, sperm or semen, and egg cells for usage in other individuals until at least 12 months after the JCAR017 infusion and until CAR T cells are no longer present by quantitative polymerase chain reaction (qPCR) on two
13. Female subjects of childbearing potential (FCBP) must:
 - Have two negative pregnancy tests as verified by the Investigator (one negative serum beta human chorionic gonadotropin [β -hCG] pregnancy test result at screening and one negative serum pregnancy test within 48 hours prior to the first dose of LD chemotherapy). Subjects must agree to have another pregnancy test performed 90 days post JCAR017 infusion. This applies even if the subject practices true

abstinence** from heterosexual contact.

Either commit to true abstinence** from heterosexual contact (which must be reviewed on a monthly basis and source documented) or agree to use, and be able to comply with, effective contraception without interruption. Contraception methods must include 1 highly effective and 1 additional effective (barrier) method of contraception from screening until at least 12 months following JCAR017 infusion and until CAR T cells are no longer present by qPCR on two consecutive tests, whichever occurs last.

Note: Highly effective methods are defined as those that result in a low failure rate (ie, less than 1% per year) when used consistently and correctly. The following are examples of highly effective and additional effective methods of contraception:

- Intrauterine device (IUD)
- Hormonal (birth control pill, injections, implants)
- Tubal ligation
- Partner's vasectomy
- Male condom (additional effective method)
- Diaphragm (additional effective method)
- Cervical cap (additional effective method)
- Agree to abstain from breastfeeding during study participation and for at least 90 days after JCAR017 infusion and until CAR T cells are no longer present by qPCR on two consecutive tests, whichever occurs last.

14. Male subjects must:

Practice true abstinence** (which must be reviewed on a monthly basis and source documented) or agree to use a condom during sexual contact with a pregnant female or a female of childbearing potential while participating in the study and until at least 12 months following JCAR017 infusion even if he has undergone a successful vasectomy and until CAR T cells are no longer present by qPCR on two consecutive tests, whichever occurs last.

** True abstinence is acceptable when this is in line with the preferred and usual lifestyle of the subject. In contrast, periodic abstinence (eg, calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception. consecutive tests, whichever occurs last.

4.3. Exclusion Criteria

The presence of any of the following will exclude a subject from enrollment:

1. Subject has any significant medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from participating in the study.
2. Subject has any condition including the presence of laboratory abnormalities, which would place the subject at unacceptable risk if participating in the study.
3. Subject has any condition that confounds the ability to interpret data from the study.
4. Subjects with T cell rich/histiocyte rich large B-cell lymphoma (THRBCL), primary cutaneous large B-cell lymphoma, primary mediastinal B-cell lymphoma (PMBCL), EBV positive DLBCL of the elderly and Burkitt lymphoma.
5. History of another primary malignancy that has not been in remission for at least 2 years

prior to enrollment. The following are exempt from the 2-year limit if curatively treated:

- Non-melanoma skin cancer
 - Localized prostate cancer
 - Cervical carcinoma in situ on biopsy or a squamous intraepithelial lesion on PAP smear
6. Treatment with any prior gene therapy product.
 7. Subjects who have received previous CD19-targeted therapy.
 8. Previous history of or active hepatitis B, hepatitis C, or human immunodeficiency virus (HIV) infection.
 9. Subjects with uncontrolled systemic fungal, bacterial, viral or other infection (including tuberculosis) despite appropriate antibiotics or other treatment at the time of leukapheresis or JCAR017 infusion.
 10. Presence of acute or chronic graft-versus-host disease (GVHD).
 11. Active autoimmune disease requiring immunosuppressive therapy.
 12. History of any one of the following cardiovascular conditions within the past 6 months:
 - Heart failure class III or IV as defined by the New York Heart Association (NYHA)
 - Cardiac angioplasty or stenting
 - Myocardial infarction
 - Unstable angina
 - Other clinically significant cardiac disease
 13. History or presence of clinically relevant CNS pathology such as epilepsy, seizure, paresis, aphasia, stroke, severe brain injuries, dementia, Parkinson's disease, cerebellar disease, organic brain syndrome, or psychosis.
 14. Treatment with alemtuzumab within 6 months of leukapheresis, or treatment with fludarabine or cladribine within 3 months of leukapheresis
 16. Use of the following (see Section 8.2 for full details):
 - Therapeutic doses of corticosteroids (defined as > 20 mg/day prednisone or equivalent) within 7 days prior to leukapheresis or 72 hours prior to JCAR017 infusion. Physiologic replacement, topical, and inhaled steroids are permitted.
 - Low-dose chemotherapy (eg, vincristine, rituximab, cyclophosphamide \leq 300 mg/m²) given after leukapheresis to maintain disease control must be stopped \geq 7 days prior to LD chemotherapy.
 - Cytotoxic chemotherapeutic agents that are not considered lymphotoxic (see below) within 1 week prior to leukapheresis. Oral anticancer agents, including lenalidomide and ibrutinib, are allowed if at least 3 half-lives have elapsed prior to leukapheresis.
 - Lymphotoxic chemotherapeutic agents (eg, cyclophosphamide, ifosfamide, bendamustine) within 2 weeks prior to leukapheresis.
 - Experimental agents within 4 weeks prior to leukapheresis unless no response or progressive disease (PD) is documented on the experimental therapy and at least 3 half-lives have elapsed prior to leukapheresis.
 - Immunosuppressive therapies within 4 weeks prior to leukapheresis and JCAR017 infusion (eg, calcineurin inhibitors, methotrexate or other chemotherapeutics, mycophenolate, rapamycin, thalidomide, immunosuppressive antibodies such as antitumor necrosis factor [TNF], anti-IL-6, or anti-IL-6R).
 - Donor lymphocyte infusions (DLI) within 6 weeks prior to JCAR017 infusion.
 - Radiation within 6 weeks prior to leukapheresis. Subjects must have progressive

disease in irradiated lesions or have additional non-irradiated, PET-positive lesions to be eligible. Radiation to a single lesion, if additional non-irradiated, measurable PET-positive lesions are present, is allowed up to 2 weeks prior to leukapheresis.

Allogeneic HSCT within 90 days prior to leukapheresis.