Study Evaluating Safety and Efficacy of JCAR017 in Subjects With Relapsed or Refractory Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL)

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Diagnosis of: 1. CLL with an indication for treatment based on the Investigator's opinion and measurable disease, or 2. SLL (lymphadenopathy and/or splenomegaly and \< 5×10\^9 CD19+ CD5+ clonal B lymphocytes/L \[\< 5000/µL\] in the peripheral blood at diagnosis with measurable disease that is biopsy-proven SLL) * Subjects (other than those in the ibrutinib + JCAR017 combination therapy and DEME cohort) must have received and failed Bruton tyrosine kinase inhibitor (BTKi) treatment or have been deemed ineligible for BTKi therapy. * Subjects in the JCAR017 monotherapy cohorts must have received previous treatment as follows: 1. Monotherapy cohorts EXCEPT DEME cohort: Subjects with CLL or SLL and high-risk features must have failed at least 2 lines of prior therapy. 2. Monotherapy cohorts EXCEPT DEME cohort: Subjects with CLL or SLL and standard-risk features must have failed at least 3 lines of prior therapy. 3. DEME cohort ONLY: Subjects with relapsed or refractory CLL or SLL, irrespective of cytogenetic risk features, must have received at least 2 lines of prior therapy including a BTKi and a BCL2i. * Subjects in the ibrutinib + JCAR017 combination therapy cohort must either: 1. be receiving ibrutinib and progressing at the time of study enrollment 2. be receiving ibrutinib for at least 6 months with a response less than complete response/remission (CR) and have high-risk features as defined in inclusion criterion 5a 3. have BTK or PLCgamma2 mutations per local laboratory assessment, with or without progression on ibrutinib 4. have previously received ibrutinib and have no contraindications to restarting ibrutinib * Eastern Cooperative Oncology Group performance status of ≤ 1 * Assessed by the Investigator to have adequate bone marrow function to receive lymphodepleting chemotherapy * Adequate organ function, defined as: 1. Serum creatinine ≤ 1.5 × age-adjusted upper limit of normal (ULN) OR calculated creatinine clearance \> 30 mL/min 2. Alanine aminotransferase ≤ 5 × ULN and total bilirubin \< 2.0 mg/dL (or \< 3.0 mg/dL for subjects with Gilbert's syndrome or leukemic infiltration of the liver) 3. Adequate pulmonary function, defined as ≤ Common Terminology Criteria for Adverse Events (CTCAE) Grade 1 dyspnea and saturated oxygen (SaO2) ≥ 92% on room air 4. Adequate cardiac function, defined as left ventricular ejection fraction ≥ 40% as assessed by echocardiogram or multiple uptake gated acquisition scan performed within 30 days prior to determination of eligibility * Subject either currently has central vascular access or is a candidate to receive central vascular access or peripheral vascular access for leukapheresis procedure. * If prior CD19-targeted therapy has been administered, subject must have CD19-positive disease confirmed by immunohistochemistry or flow cytometry since completing the prior CD19-targeted therapy. * Subjects in ibrutinib + JCAR017 combination cohort must have progressed on a BTKi and have received prior therapy with venetoclax * Subjects in venetoclax + JCAR017 combination cohort must: 1. have failed at least 1 prior line of therapy, including failed BTKi therapy or have been deemed ineligible to receive BTKi 2. be venetoclax naive (required for dose expansion) or 3. if prior venetoclax (only for dose escalation) 4. have no contraindictions to re-initiation of venetoclax based on prior intolerance and have had at least 6 months elapsed since the last dose of venetoclax, if either, best response was stable disease, or subject experienced disease progression on venetoclax, or within 6 months of venetoclax discontinuation * subjects in the venetoclax + JCAR017 combination must have hemoglobin \>=9 g/dL, absolute neutrophil count \>=500mm3 and platelets\>= 75,000/mm3, unless cytopenias are judged by investigator to be due to CLL infiltration of the bone marrow * must have diagnosis of CLL or SLL with an indication for treatment based on the investigator's opinion and measurable disease (any of the following measurable lymph nodes ≥1.5 cm in the greatest transverse diameter and/or hepatomegaly or splenomegaly) and demonstration of CLL cells in the peripheral blood by flow cytometry

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Exclusion Criteria:

* Subjects with known active central nervous system (CNS) involvement by malignancy. Those with prior CNS disease that has been effectively treated will be eligible if treatment was completed at least 3 months prior to enrollment with no evidence of symptomatic disease and stable abnormalities on repeat imaging. * History of another primary malignancy that has not been in remission for at least 2 years. (The following are exempt from the 2-year limit: nonmelanoma skin cancer, completely resected stage 1 solid tumor with low risk for recurrence, curatively treated localized prostate cancer, cervical carcinoma in situ on biopsy or a squamous intraepithelial lesion on Pap smear, and in situ breast cancer that has been completely resected.) * Subjects with Richter's transformation * Prior treatment with any gene therapy product * Active hepatitis B, active hepatitis C, or active human immunodeficiency virus (HIV) infection * Systemic fungal, bacterial, viral, or other infection that is not controlled * Presence of acute or extensive chronic graft versus host disease (GVHD) * History of any one of the following cardiovascular conditions within the past 6 months: Class III or IV heart failure as defined by the New York Heart Association (NYHA), cardiac angioplasty or stenting, myocardial infarction, unstable angina, or other clinically significant cardiac disease * History or presence of clinically relevant CNS pathology such as epilepsy, generalized seizure disorder, aphasia, stroke with current neurologic sequelae, severe brain injuries, dementia, Parkinson's disease, cerebellar disease,cerebral edema, or psychosis * Pregnant or nursing (lactating) women * Use of any of the following medications or treatments within the noted time prior to leukapheresis: 1. Alemtuzumab within 6 months prior to leukapheresis 2. Allogeneic hematopoietic stem cell transplant within 100 days prior to leukapheresis 3. Cladribine within 3 months prior to leukapheresis 4. Donor lymphocyte infusions (DLI) within 2 months prior to leukapheresis 5. Radiation including large bone marrow fields such as sternum or pelvis within 6 weeks prior to leukapheresis 6. Fludarabine within 4 weeks prior to leukapheresis 7. GVHD therapies such as calcineurin inhibitors, methotrexate or other chemotherapeutics, mycophenolate mofetil, rapamycin, or immunosuppressive antibodies (such as anti-tumor necrosis factor-α \[TNFα\], anti-interleukin-6 \[IL-6\], or anti-interleukin-6 receptor \[IL 6R\]) within 4 weeks prior to leukapheresis 8. Cyclophosphamide, ifosfamide, bendamustine, chlorambucil, or melphalan within 2 weeks prior to leukapheresis 9. Therapeutic doses of corticosteroids (defined as \> 20 mg/day prednisone or equivalent) within 7 days prior to leukapheresis 10. Anti-CD20 monoclonal antibodies within 7 days prior to leukapheresis 11. Venetoclax within 4 days prior to leukapheresis 12. Idelalisib or duvelisib within 2 days prior to leukapheresis 13. Lenalidomide or covalent and non-covalent BTKi within 1 day prior to leukapheresis 14. Experimental agents, including off-label use of approved drugs (with the exception of acalabrutinib which may be continued up to the day before leukapheresis), within 4 weeks prior to leukapheresis unless progression is documented on the experimental therapy and at least 3 half-lives have elapsed prior to leukapheresis * Uncontrolled medical, psychological, familial, sociological, or geographical conditions that do not permit compliance with the protocol, as judged by the Investigator; or subject unwillingness or inability to follow the procedures required in the protocol * Progressive vascular tumor invasion, thrombosis, or embolism * Deep vein thrombosis or embolism not managed on a stable regimen of anticoagulation * Use of any of the following medications or treatments within the noted time prior to leukapheresis lenalidomide or acalabrutinib within 1 day prior to leukapheresis experimental agents, including off-label use of approved drugs, within 4 weeks prior to leukapheresis. * Venous thrombosis or embolism requiring treatment but not managed on a stable regimen of anticoagulation * For subjects in the venetoclax + JCAR017 combination cohorts only, concomitant treatment with CYP3A moderate/strong inducers or moderate/strong inhibitors which cannot be discontinued

Conditions & Interventions

Interventions:

BIOLOGICAL: JCAR017 (lisocabtagene maraleucel), BIOLOGICAL: JCAR017 (lisocabtagene maraleucel) + ibrutinib, BIOLOGICAL: JCAR017 (lisocabtagene maraleucel) + venetoclax

Conditions:

Leukemia, Lymphocytic, Chronic, B-Cell, Lymphoma, Small Lymphocytic

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Keywords:
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More Information

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