A Study to Evaluate the Efficacy and Safety of JCAR017 in Adult Subjects With Relapsed or Refractory Indolent B-cell Non-Hodgkin Lymphoma (NHL)

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT04245839	RECRUITING	JANUARY 29, 2020	NOVEMBER 16, 2021

STUDY DESCRIPTION

Brief Summary

This is a global Phase 2, open-label, single-arm, multicohort, multicenter study to evaluate efficacy and safety of JCAR017 in adult subjects with r/r FL or MZL. The study will be conducted in compliance with the International Council on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use/Good Clinical Practice (GCP) and applicable regulatory requirements. This study is divided into three periods: Pretreatment, which consists of screening assessments, leukapheresis and the Pretreatment evaluation; Treatment, which starts with the administration of lymphodepleting (LD) chemotherapy and continues through JCAR017 administration at Day 1 with follow-up through Day 29; Posttreatment, which includes follow-up assessments for disease status and safety for 2 years.

Condition or Disease: Lymphoma, Non-Hodgkin

Intervention/treatment: Drug: Fludarabine
Drug: Cyclophosphamide
Drug: JCAR017

Phase: Phase 2

DETAILED DESCRIPTION

N/A

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 188 participants

Intervention Model : Single Group Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Phase 2, Open-label, Single Arm, Multicenter Trial to Evaluate the Safety and Efficacy of JCAR017 (Lisocabtagene Maraleucel) in Adult Subjects With High-risk, Relapsed or Refractory Indolent B-cell Non-Hodgkin Lymphoma (NHL)

Actual Study Start Date: July 2020

Estimated Primary Completion Date: April 2024

Estimated Study Completion Date: April 2024

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: Administration of JCAR017 Subjects will be treated with fludarabine IV (30 mg/m2/day for 3 days) and cyclophosphamide IV (300 mg/m2/day for 3 days) prior to JCAR017 infusion. Refer to the most recent package inserts for further details on administration of these agents. JCAR017 will be infused on Day 1 at a dose of 100 × 10^6 CAR-positive viable T cells (CAR+ T cells), 2 to 7 days after completion of LD chemotherapy. Each JCAR017 dose includes CD4+ CAR+ T cells and CD8+ CAR+ T cells.	Drug: Fludarabine Fludarabine Drug: Cyclophosphamide Cyclophosphamide Drug: JCAR017 JCAR017

OUTCOME MEASURES

Primary Outcome Measures:
1. Overall Response Rate (ORR) [Time Frame: Up to 24 months]
Is defined as the percentage of participants achieving either a partial response (PR) or complete response (CR) at any time up to 24 months after JCAR017 treatment as assessed by PET-CT and/or CT using "The Lugano classification"

Secondary Outcome Measures:
1. Complete response rate (CRR) as assessed but PET-CT and/or CT using "The Lugano Classification" [Time Frame: Up to 24 months]
Is defined as the percentage of subjects achieving a CR at any time up to 24 months after JCAR017 treatment
2. Duration of Response (DOR) if Best Overall Response (BOR) is CR, as assessed by PET-CT and/or CT using "The Lugano Classification" [Time Frame: Up to 24 months]
is defined for subjects with a BOR of CR as the time from first response (CR or PR) to disease progression or death from any cause up to 24 months after JCAR017 treatment
3. Duration of Response (DOR) as assessed by PET-CT and/or CT using "The Lugano Classification" [Time Frame: Up to 24 months]
is defined as the time from first response (CR or PR) to disease progression or death from any cause, whichever occurs first up to 24 months after JCAR017 treatment
4. Progression-Free Survival (PFS) as assessed by PET-CT and/or CT using "The Lugano Classification" [Time Frame: Up to 24 months]
is defined as the time from start of JCAR017 to disease progression or death from any cause, whichever occurs first up to 24 months after JCAR017 treatment

5. Overall Survival (OS) [Time Frame: Up to 24 months]
is defined as the time from start of JCAR017 to time of death due to any cause up to 24 months after JCAR017 treatment
6. Adverse Events (AEs) [Time Frame: Up to 24 months]
An AE is any noxious, unintended, or untoward medical occurrence that may appear or worsen in a subject during the course of a study. It may be a new intercurrent illness, a worsening concomitant illness, an injury, or any concomitant impairment of the subject's health, including laboratory test values, regardless of etiology. Any worsening (ie, any clinically significant adverse change in the frequency or intensity of a preexisting condition) should be considered an AE.
7. Pharmacokinetics - Cmax [Time Frame: Up to 24 months]
Maximum concentration
8. Pharmacokinetics - Tmax [Time Frame: Up to 24 months]
Time to maximum concentration
9. Pharmacokinetics - AUC [Time Frame: Up to 24 months]
Area under the curve
10. European Organization for Research and Treatment of Cancer - Quality of Life C30 questionnaire (EORTC QLQ-C30) [Time Frame: Up to 24 months]
is questionnaire that will be used as a measure of health-related quality of life. The EORTC QLQ-C30 is composed of both multi-item scales and single item measures. These include five functional scales (physical, role, emotional, cognitive and social), three symptom scales (fatigue, nausea/vomiting, and pain), a global health status/health-related quality of life (HRQoL) scale, and six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). Each of the multi-item scales includes a different set of items - no item occurs in more than one scale.
11. Functionality Assessment of Cancer Therapy Lymphoma Subscale (FACT-LymS) [Time Frame: Up to 24 months]
is a 15-item lymphoma-specific additional concerns subscale. This subscale addresses symptoms and functional limitations are important to lymphoma patients. The FACT-LymS items are scored on a 0 ("Not at all") to 4 ("Very much") response scale. Items are aggregated to a single score on a 0-60 scale. High scores indicate lower symptom burden.

ELIGIBILITY CRITERIA

Ages Eligible for Study: 18 Years and older (Adult, Older Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:
Relapsed or refractory follicular lymphoma (FL) (Grade 1, 2 or 3a) or marginal zone lymphoma (MZL) histologically confirmed within 6 months of screening, as assessed by local pathology Patients should have received at least one prior therapy that includes anti-CD20 and alkylating agent Follicular lymphoma patients: Received at least one prior line of systemic therapy. Patients that received one prior line of systemic therapy are eligible if they present with high risk features. Patients that received two or more prior lines of systemic therapy are eligible, assuming one of the prior lines includes anti-CD20 and alkylating agent (as listed in criterion 2) Marginal zone lymphoma patients: Received two or more prior lines of systemic therapy, assuming one of the prior lines includes anti-CD20 and alkylating agent (as listed in criterion 2) or relapsed after hematopoietic stem cell transplant Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 Adequate organ function Adequate vascular access for leukapheresis procedure
Exclusion Criteria:
Evidence or history of composite Diffuse large B-cell lymphoma (DLBCL) and FL, or of transformed FL WHO subclassification of duodenal-type FL Central nervous system-only involvement by malignancy (subjects with secondary central nervous system (CNS) involvement are allowed on study) History of another primary malignancy that has not been in remission for at least 2 years, with the exception of non-invasive malignancies Prior CAR T-cell or other genetically-modified cell therapy History of or active human immunodeficiency virus (HIV) Active hepatitis B or active hepatitis C Uncontrolled systemic fungal, bacterial, viral or other infection despite appropriate antibiotics or other treatment Active autoimmune disease requiring immunosuppressive therapy Presence of acute or chronic graft-versus-host=disease History of significant cardiovascular disease History or presence of clinically relevant central nervous system pathology Allogenic-hematopoietic stem cell transplant (Allo-HSCT) within 90 days of leukapheresis

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CONTACTS AND LOCATIONS

Contacts

Contact: Recruiting sites have contact information. Please contact the sites directly. If there is no contact information, please email: Clinical.Trials@bms.com
Contact: First line of the email MUST contain NCT # and Site #.

Locations

United States, California	UCLA Medical Centre-Santa Monica	Santa Monica
United States, Colorado	University of Colorado Cancer Center	Aurora
United States, Connecticut	Yale New Haven Health - Smilow Cancer Hospita	New Haven
United States, Illinois	Northwestern University - Robert H. Lurie Comprehensive Cancer Center	Chicago
United States, Illinois	Illinois Cancer Specialists - Arlington Heights	Niles
United States, Maryland	University of Maryland - Greenebaum Comprehensive Cancer Center	Baltimore
United States, Massachusetts	Massachusetts General Hospital - Dana-Farber Cancer Institute (The Jon and JoAnn Hagler Center for Lymphoma)	Boston
United States, Massachusetts	Beth Israel Deaconess Medical Center	Boston
United States, New York	Memorial Sloan Kettering Cancer Center	New York
United States, North Carolina	Novant Health Cancer Specialists Charlotte	Charlotte
United States, Ohio	Cleveland Clinic - Taussig Cancer Institute	Cleveland
United States, Oregon	Providence Cancer Center - Earle A. Chiles Research Institute	Portland

United States, Pennsylvania	Perelman Center for Advanced Medicine - Abramson Cancer Center University of Pennsylvania	Philadelphia
United States, South Dakota	Avera Research Institute	Sioux Falls
United States, Texas	The University of Texas - MD Anderson Cancer Center	Houston
United States, Virginia	University of Virginia Health System	Charlottesville
United States, Washington	Fred Hutchinson Cancer Research Center	Seattle
Austria	Allgemeinen Krankenhaus (AKH) Wien - Medizinische Universitaet Wien	Wien
Canada, Montreal	Hospital Maisonneuve - Rosemont	Quebec
Canada, Toronto	Princess Margaret Cancer Centre	Ontario
Canada	CIUSSS de l'Est-de-l'Ile-de-Montreal - Installation Hopital Maisonneuve-Rosemont	Quebec
France	CHRU-Hopital Claude Huriez	Lille
France	CHU Montpellier - Hôpital Saint Eloi	Montpellier
France	Centre Hospitalier Lyon-Sud	Pierre-Benite
Germany	Universitatsklinikum Koeln	Koeln
Germany	LMU Klinikum der Universitat Muenchen	Munich
Germany	Universitaetsklinikum Ulm	Ulm
Italy	Azienda Ospedaliera Papa Giovanni XXIII	Bergamo
Italy	Istituto Nazionale Per Lo Studio E La Cura Dei Tumori Fondazione Giovanni Pascale	Naples
Japan	National Cancer Center Hospital	Chuo-ku
Japan	Kyushu University Hospital	Fukuoka
Japan	Toranomon Hospital	Minato-ku
Japan	Hokkaido University Hospital	Sapporo-shi, Hokkaido
Spain	Universitario de Salamanca - Hospital Clinico	Salamanca
Spain	Hospital Universitario Virgen del Rocio	Sevilla
Sweden	Karolinska University Hospital	Stockholm
United Kingdom	University College London Hospitals NHS Foundation Trust - University College Hospital	London
United Kingdom	The Christie NHS Foundation Trust	Withington

Sponsors and Collaborators

Celgene

Investigator

Study Director :	Thalia Farazi, M.D./Ph.D	Celgene Medical Director

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MORE INFORMATION

Responsible Party :	Celgene
ClinicalTrials.gov Identifier :	NCT04245839
Other Study ID Numbers :	JCAR017-FOL-001, U1111-1244-9768, 2019-004081-18
First Posted :	January 29, 2020
Last Update Posted :	November 16, 2021
Last Verified :	November 2021
Individual Participant Data (IPD) Sharing Statement:	
Plan to Share IPD:	Yes
Plan Description:	Information relating to our policy on data sharing and the process for requesting data can be found at the following link: https://www.celgene.com/research-development/clinical-trials/clinical-trials-data-sharing/
Supporting Materials:	Study Protocol, Statistical Analysis Plan (SAP), Informed Consent Form (ICF), Clinical Study Report (CSR), Analytic Code
Time Frame:	See Plan Description
Access Criteria:	See Plan Description

URL:	https://www.celgene.com/research-development/clinical-trials/clinical-trials-data-sharing/
Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
Keywords provided by Celgene:	*B-cell Non-Hodgkin Lymphoma (NHL)* *JCAR017 Relapsed or Refractory*
Additional relevant MeSH terms :	*Lymphoma* *Lymphoma, Non-Hodgkin* *Lymphoma, B-Cell* *Neoplasms by Histologic Type* *Neoplasms* *Lymphoproliferative Disorders* *Lymphatic Diseases* *Immunoproliferative Disorders* *Immune System Diseases*