A Study to Compare the Efficacy and Safety of JCAR017 to Standard of Care in Adult Subjects With High-risk, Transplant-eligible Relapsed or Refractory Aggressive B-cell Non-Hodgkin Lymphomas

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT03575351	RECRUITING	JULY 2, 2018	AUGUST 31, 2020

STUDY DESCRIPTION

Brief Summary

The study will be conducted in compliance with the International Council for Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use/Good Clinical Practice (GCP) and applicable regulatory requirements. This is a randomized, open-label, parallel-group, multi-center trial in adult subjects with Relapsed or refractory (R/R) aggressive Non-Hodgkin lymphoma (NHL) to compare safety and efficacy between the standard of care (SOC) strategy versus JCAR017 (also known as lisocabtagene maraleucel or liso-cel). Subjects will be randomized to either receive SOC (Arm A) or to receive JCAR017 (Arm B). All subjects randomized to Arm A will receive Standard of care (SOC) salvage therapy (R-DHAP, RICE or R-GDP) as per physician's choice before proceeding to High dose chemotherapy (HDCT) and Hematopoietic stem cell transplant (HSCT). Subjects from Arm A may be allowed to cross over and receive JCAR017 upon confirmation of an EFS event. Subjects randomized to Arm B will receive Lymphodepleting (LD) chemotherapy followed by JCAR017 infusion.

Condition or Disease: Lymphoma, Non-Hodgkin

Intervention/treatment: Genetic: JCAR017
Drug: Standard of Care

Phase: Phase 3

DETAILED DESCRIPTION

N/A

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 182 participants

Intervention Model : Parallel Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Global Randomized Multicenter Phase 3 Trial of JCAR017 Compared to Standard of Care in Adult Subjects With High-risk, Second-line, Transplant-eligible Relapsed or Refractory Aggressive B-cell Non-Hodgkin Lymphomas (TRANSFORM).

Actual Study Start Date: October 2018

Estimated Primary Completion Date: January 2024

Estimated Study Completion Date: January 2024

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Active Comparator: Arm A - Standard of Care (SOC) Subjects should receive SOC (R-DHAP, R-ICE or R-GDP) followed by HDCT (BEAM) and HSCT. Standard of care regimen will be administered as per investigator decision.	Drug: Standard of Care Standard of Care
Experimental: Arm B - JCAR017 Lymphodepleting chemotherapy with intravenous (IV) fludarabine (30 mg/m2/day for 3 days) plus cyclophosphamide IV (300 mg/m2/day for 3 days) (flu/cy) concurrently followed by JCAR017 infusion.	Genetic: JCAR017 JCAR017

OUTCOME MEASURES

Primary Outcome Measures:
1. Event-free survival (EFS) [Time Frame: Approximately 3 years]
Time from randomization to death from any cause, progressive disease (PD), failure to achieve complete response (CR) or partial response (PR), or start of new antineoplastic therapy due to efficacy concerns, whichever occurs first

Secondary Outcome Measures:
1. Complete response rate (CRR) [Time Frame: Approximately 3 years]
Percentage of subjects achieving a complete response (CR)
2. Progression-free survival (PFS) [Time Frame: Approximately 3 years]
Time from randomization to PD or death from any cause, whichever occurs first
3. Overall survival (OS) [Time Frame: Approximately 4.5 years]
Time from randomization to time of death due to any cause
4. Overall response rate (ORR) [Time Frame: Approximately 3 years]
Percentage of subjects achieving an objective response of partial response (PR) or better according to the Lugano Classification as assessed by IRC review

5. Duration of response (DOR) [Time Frame: Approximately 3 years]
Time from first response to disease progression, start of new antineoplastic therapy due to efficacy concerns or death from any cause
6. PFS on next line of treatment (PFS-2) [Time Frame: Approximately 3 years]
Time from randomization to second objective disease progression or death from any cause, whichever is first.
7. Adverse Events (AEs) [Time Frame: Approximately 3 years]
Type, frequency and severity of adverse events (AEs), serious adverse events (SAE), and laboratory abnormalities (overall and in clinical, histological and molecular subgroups)
8. HRQoL using European Organisation for Research and Treatment of Cancer - Quality of Life C30 questionnaire (EORTC-QLQ-C30) [Time Frame: Approximately 3 years]
European Organisation for Research and Treatment of Cancer - Quality of Life C30 questionnaire: The EORTC QLQ-C30 questionnaire will be used as a measure of health-related quality of life, fatigue, physical and cognitive functions.
9. HRQoL parameters assessed by FACT-Lym "Additional concerns" subscale [Time Frame: Approximately 3 years]
Functional Assessment of Cancer Therapy-Lymphoma "Additional concerns" subscale: Only the LYM subscale will be administered in this study. This scale addresses symptoms and functional limitations (15 item) that are important to lymphoma patients.
10. Reasons for hospital resource utilization [Time Frame: Approximately 3 years]
Will be assessed based on reasons for hospitalization
11. Rate of hematopoietic stem cell transplant (HSCT) [Time Frame: Approximately 3 years]
Rate of completion of HDCT and HSCT
12. Frequency of hospital resource utilization [Time Frame: Approximately 3 years]
Will be assessed based on frequency of hospitalizations calculated as, inpatient days, intensive care unit (ICU) days, outpatient visits days
13. Hospital resource utilization (HRU) [Time Frame: Approximately 3 years]
Will be assessed based on frequency of hospitalizations calculated as, inpatient days, intensive care unit (ICU) days, outpatient visits days and reasons for hospitalization

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ELIGIBILITY CRITERIA

Ages Eligible for Study: 18 to 75 Years (Adult, Older Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:
1. Subject is ≥ 18 years and ≤ 75 years of age at the time of signing the informed consent form (ICF).
2. Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1.
3. Histologically proven diffuse large B-cell lymphoma (DLBCL) NOS (de novo or transformed indolent NHL), high grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements with DLBCL histology (double/triple-hit lymphoma [DHL/THL]), primary mediastinal (thymic) large B-cell lymphoma (PMBCL), T cell/histiocyte-rich large B-cell lymphoma (THRBCL) or follicular lymphoma grade 3B. Enough tumor material must be available for confirmation by central pathology.
4. Refractory or relapsed within 12 months from CD20 antibody and anthracycline containing first line therapy.
5. [18F] fluorodeoxyglucose (FDG) positron emission tomography (PET) positive lesion at screening. (Deauville score 4 or 5)
6. Adequate organ function
7. Participants must agree to use effective contraception
Exclusion Criteria:
1. Subjects not eligible for hematopoietic stem cell transplantation (HSCT).
2. Subjects planned to undergo allogeneic stem cell transplantation.
3. Subjects with, primary cutaneous large B-cell lymphoma, EBV (Epstein-Barr virus) positive DLBCL, Burkitt lymphoma or transformation from chronic lymphocytic leukemia/small lymphocytic lymphoma (Richter transformation).
4. Subjects with prior history of malignancies, other than aggressive R/R NHL, unless the subject has been free of the disease for ≥ 2 years with the exception of the following noninvasive malignancies:
- Basal cell carcinoma of the skin
- Squamous cell carcinoma of the skin
- Carcinoma in situ of the cervix
- Carcinoma in situ of the breast
- Incidental histologic finding of prostate cancer (T1a or T1b using the TNM [tumor, nodes, metastasis] clinical staging system) or prostate cancer that is curative.
- Other completely resected stage 1 solid tumor with low risk for recurrence
5. Treatment with any prior gene therapy product.
6. Subjects who have received previous CD19-targeted therapy.
7. Subjects with active hepatitis B, or active hepatitis C are excluded. Subjects with negative polymerase chain reaction (PCR) assay for viral load for hepatitis B or C are permitted. Subjects positive for hepatitis B surface antigen and/or anti-hepatitis B core antibody with negative viral load are eligible and should be considered for prophylactic antiviral therapy. Subjects with a history of or active human immunodeficiency virus (HIV) are excluded.
8. Subjects with uncontrolled systemic fungal, bacterial, viral or other infection (including tuberculosis) despite appropriate antibiotics or other treatment.
9. Active autoimmune disease requiring immunosuppressive therapy.
10. History of any one of the following cardiovascular conditions within the past 6 months prior to signing the ICF: 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.
11. History or presence of clinically relevant central nervous system (CNS) pathology
12. Pregnant or nursing (lactating) women.

CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

United States, Arizona	Virginia G Piper Cancer Center	Scottsdale
United States, Arizona	Mayo Clinic Arizona	Scottsdale

United States, California	University of California San Francisco	San Francisco
United States, Colorado	University of Colorado Cancer Center	Aurora
United States, Florida	Mayo Clinic - Jacksonville	Jacksonville
United States, Florida	H. Lee Moffitt Cancer Center and Research Institute	Tampa
United States, Georgia	Emory University	Atlanta
United States, Georgia	Blood and Marrow Transplant Group of Georgia	Atlanta
United States, Illinois	Northwestern University-Feinberg School of Medicine	Chicago
United States, Illinois	Loyola University Medical Center Cardinal Bernardin Cancer Center	Maywood
United States, Massachusetts	Massachusetts General Hospital / Dana-Farber Cancer Institute	Boston
United States, Massachusetts	Beth Israel Deaconess Medical Center	Boston
United States, Michigan	University of Michigan	Ann Arbor
United States, Michigan	Barbara Ann Karmanos Cancer Center	Detroit
United States, Minnesota	University of Minnesota	Minneapolis
United States, Minnesota	Mayo Clinic - Rochester	Rochester
United States, Nebraska	University of Nebraska Medical Center	Omaha
United States, New Jersey	John Theurer Cancer Center at Hackensack University Medical Center	Hackensack
United States, New York	Roswell Park Cancer Institute	Buffalo
United States, New York	Memorial Sloan Kettering Cancer Center	New York
United States, North Carolina	Levine Cancer Institute	Charlotte
United States, Oklahoma	University of Oklahoma Peggy and Charles Stephenson Cancer Center	Oklahoma City
United States, Oregon	Oregon Health and Science University	Portland
United States, Pennsylvania	Hillman Cancer Institute at UPMC	Pittsburgh
United States, Texas	Baylor University Medical Center	Dallas
United States, Texas	The University of Texas - MD Anderson Cancer Center	Houston
United States, Virginia	Virginia Commonwealth University	Richmond
United States, Washington	Fred Hutchinson Cancer Research Center	Seattle
Belgium	UZ Gent	Gent
France	CHRU-Hopital Claude Huriez	Lille
France	Institut Paoli Calmette Hematologie	Marseille cedex
France	Centre Hospitalier Lyon Sud	Pierre Benite
France	Gustave Roussy	Villejuif CEDEX
Germany	Robert-Rössle-Klinik im HELIOS Klinikum Berlin-Buch Klinik für Hämatologie, Onkologie u. Tumorimmuno	Berlin
Germany	Universitaetsklinikum Carl Gustav Carus	Dresden
Germany	Universitaetsklinik Hamburg - Eppendorf	Hamburg
Germany	Universitat zu Koln	Köln
Germany	Universitatsklinik Muenster	Muenster
Germany	LMU Klinikum der Universitat	München
Italy	La Sapienza, University of Rome	Rome
Italy	Istituto Clinico Humanitas	Rozzano (MI)
Italy	Azienda Ospedaliera Citta della Salute e della Scienza di Torino	Torino
Japan	Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital	Bunkyo-ku
Japan	National Cancer Center Hospital	Chuo-ku
Japan	Toranomon Hospital	Minato-ku
Japan	Osaka City University Hospital	Osaka
Netherlands	Erasmus Medical Center-Daniel den Hoed	Rotterdam

Spain	Hospital Clinic i Provincial de Barcelona - ICMHO	Barcelona
Spain	Hospital Universitario 12 de Octubre	Madrid
Sweden	Karolinska Universitetssjukhuset - Huddinge	Stockholm
Switzerland	Universitatsspital Bern	Bern
United Kingdom	UCL Cancer Institute	London
United Kingdom	University Hospital Southampton NHS Foundation Trust - Southampton General Hospital	Southampton

Sponsors and Collaborators

Celgene

Investigator

Study Director : Alessandro Crotta, MD Celgene

MORE INFORMATION

Responsible Party :	Celgene
ClinicalTrials.gov Identifier :	NCT03575351
Other Study ID Numbers :	JCAR017-BCM-003, U1111-1213-1944, 2018-000929-32
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Last Verified :	August 2020
Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
Keywords provided by Celgene:	*Safety* *JCAR017* *Liso-cel* *Relapsed* *Non-Hodgkin Lymphomas DLBCL* *Efficacy* *High-Risk* *Refractory* *B-cell NHL*
Additional relevant MeSH terms :	*Lymphoma* *Lymphoma, B-Cell* *Lymphoma, Non-Hodgkin*