Study Evaluating the Safety and Pharmacokinetics of JCAR017 in B-cell Non-Hodgkin Lymphoma (TRANSCEND-NHL-001)

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT02631044	RECRUITING	DECEMBER 15, 2015	AUGUST 2, 2022

STUDY DESCRIPTION

Brief Summary

This open-label Phase 1 study will evaluate the safety, PK, and antitumor activity of modified T cells (JCAR017) administered to adult patients with relapsed or refractory B-cell NHL. The dose and schedule of JCAR017 will be evaluated and modified, as needed, for safety and antitumor activity. We will also determine how long the modified T cells stay in the patient's body and how well JCAR017 works in treating patients with non-Hodgkin's lymphoma whose disease has come back or has not responded to treatment.

Condition or Disease: Non-Hodgkin Lymphoma
Diffuse Large B Cell Lymphoma
Follicular Lymphoma
Mantle-cell Lymphoma
Primary Mediastinal B-cell Lymphoma

Intervention/treatment: Biological: JCAR017 (lisocabtagene maraleucel) single-dose schedule
Biological: JCAR017 (lisocabtagene maraleucel) 2-dose schedule

Phase: Phase 1

DETAILED DESCRIPTION

This is an open-label, multicenter Phase 1 study to determine the safety, pharmacokinetics (PK), and antitumor activity of JCAR017 in adult patients with relapsed or refractory diffuse large B cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL), follicular lymphoma Grade 3B, and mantle cell lymphoma (MCL). This study will evaluate and refine the dose and schedule of JCAR017 to optimize safety and antitumor activity. A dose-confirmation group or groups will further evaluate the safety and efficacy of JCAR017 at the recommended regimen(s).
Upon successful generation of JCAR017 product, participants will receive treatment with one or more cycles of JCAR017 therapy. Each cycle will include lymphodepleting chemotherapy followed by one or two doses of JCAR017 administered by intravenous (IV) injection.
The follow-up period for each participant is approximately 24 months after the final JCAR017 infusion. Long-term follow-up for survival, toxicity, and viral vector safety will continue under a separate long-term follow-up protocol per health regulatory authority guidelines, currently up to 15 years after the last JCAR017 infusion.

STUDY DESIGN

Study Type: Interventional
Estimated Enrollment : 314 participants
Allocation : Non-Randomized
Intervention Model : Parallel Assignment
Masking: None (Open Label) ()
Primary Purpose: Treatment
Official Title: Study Evaluating the Safety and Pharmacokinetics of JCAR017 in B-cell Non-Hodgkin Lymphoma (TRANSCEND-NHL-001)

Actual Study Start Date: January 2016
Estimated Primary Completion Date: December 2022
Estimated Study Completion Date: December 2022

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: JCAR017 1-dose schedule Each cycle of JCAR017 (lisocabtagene maraleucel) will be administered as 1 intravenous (IV) injection	Biological: JCAR017 (lisocabtagene maraleucel) single-dose schedule Participants will undergo leukapheresis to isolate peripheral blood mononuclear cells (PBMCs) for the production of JCAR017. During JCAR017 production, participants may receive low-dose chemotherapy for disease control. Upon successful generation of JCAR017 product, participants will receive treatment with JCAR017 therapy. Treatment will include lymphodepleting chemotherapy followed by one dose of JCAR017 administered by intravenous (IV) injection.
Experimental: JCAR017 2-dose schedule (no longer accruing) Each cycle of JCAR017 (lisocabtagene maraleucel) will be administered as 2 intravenous (IV) injections	Biological: JCAR017 (lisocabtagene maraleucel) 2-dose schedule Participants will undergo leukapheresis to isolate peripheral blood mononuclear cells (PBMCs) for the production of JCAR017. During JCAR017 production, participants may receive low-dose chemotherapy for disease control. Upon product availability, participants will receive study treatment consisting of lymphodepleting chemotherapy followed by two IV doses of JCAR017.

OUTCOME MEASURES

Primary Outcome Measures:	1. Treatment-related adverse events (AEs) as assessed by CTCAE v4.03 [Time Frame: Up to 730 days after the final JCAR017 infusion] Physiological parameter 2. Dose-limiting toxicities of JCAR017 [Time Frame: 28 days after first (single-dose schedule) or second (2-dose schedule) JCAR017 infusion] Physiological parameter 3. Objective response rate (ORR) [Time Frame: 24 months] Lugano criteria
Secondary Outcome Measures:	1. Complete response (CR) rate [Time Frame: 24 months] Lugano criteria 2. Duration of response [Time Frame: 24 months] Lugano criteria 3. Progression-free survival (PFS) [Time Frame: 24 months] Lugano criteria 4. Overall survival [Time Frame: Up to 15 years] Physiological parameter 5. Health-related quality of life [Time Frame: 24 months] Questionnaire 6. Maximum concentration of JCAR017 (Cmax) in the peripheral blood [Time Frame: Up to 365 days after the final JCAR017 infusion] qPCR 7. Time to maximum concentration of JCAR017 (Tmax) in the peripheral blood [Time Frame: Up to 365 days after the final JCAR017 infusion] qPCR 8. Area-under-the-concentration-vs-time-curve (AUC) in the peripheral blood [Time Frame: Up to 365 days after the final JCAR017 infusion] qPCR

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:
Age ≥18 years
Relapsed or refractory B-cell NHL, including
DLBCL cohort (no longer enrolling): DLBCL, not otherwise specified (NOS; includes transformed DLBCL from indolent histology [tDLBCL]), high-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements with DLBCL histology (Swerdlow 2016), primary mediastinal B-cell lymphoma (PMBCL), and follicular lymphoma Grade 3B. Subjects must have been treated with an anthracycline and rituximab (or other CD20-targeted agent) and have relapsed or refractory disease after at least 2 lines of systemic therapy or after auto-HSCT. MCL cohort: MCL (diagnosis must be confirmed with cyclin D1 expression or evidence of t(11;14) by cytogenetics, fluorescent in situ hybridization [FISH], or PCR) with relapsed or refractory disease after at least 2 prior lines of systemic MCL therapy. Subjects must have been treated with an alkylating agent, Bruton's tyrosine kinase inhibitor (BTKi), and rituximab (or other CD20-targeted agent). PET-positive disease by Lugano classification Archived tumor biopsy tissue available from the last relapse and corresponding pathology report available or, if at least one tumor-involved site is deemed accessible at time of screening, willing to undergo pre-treatment biopsy (excisional when possible) for disease confirmation. If a subject has never had a complete response, a sample from the most recent biopsy is acceptable. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 Adequate bone marrow, renal, hepatic, pulmonary, and cardiac function Adequate vascular access for leukapheresis procedure Participants who have received previous CD19-targeted therapy must have CD19-positive lymphoma confirmed on a biopsy since completing the prior CD19-targeted therapy. Participants must agree to use appropriate contraception.
Exclusion Criteria:
Active central nervous system (CNS)-only involvement by malignancy (note: participants with secondary CNS involvement are allowed on study) History of other primary malignancy not in remission for at least 2 years (The following are exempt from the 2-year limit: nonmelanoma skin cancer, definitively treated stage 1 solid tumor with low risk for recurrence, curatively treated localized prostate cancer, and cervical carcinoma in situ on biopsy or a squamous intraepithelial lesion on Pap smear) Treatment with alemtuzumab within 6 months of leukapheresis or fludarabine or cladribine within 3 months of leukapheresis Active hepatitis B, hepatitis C, or Subjects with a history of or active human immunodeficiency virus (HIV) infectionare excluded. Subjects with active hepatitis B, or active hepatitis C are also excluded. Subjects with a negative 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 Uncontrolled systemic fungal, bacterial, viral, or other infection Presence of graft-vs-host disease (GVHD) History of cardiovascular disease 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 Pregnant or nursing women
Use of the following:
Therapeutic doses of corticosteroids (defined as >20 mg/day prednisone or equivalent) within 7 days of leukapheresis or 72 hours prior to JCAR017 administration. Physiologic replacement, topical, and inhaled steroids are permitted. Low dose chemotherapy (e.g., vincristine, rituximab, cyclophosphamide ≤300 mg/m2) given after leukapheresis to maintain disease control must be stopped ≥7 days prior to lymphodepleting chemotherapy. Cytotoxic chemotherapeutic agents that are not considered lymphotoxic (see below) within 1 week of leukapheresis. Oral chemotherapeutic agents, including lenalidomide and ibrutinib, are allowed if at least 3 half-lives have elapsed prior to leukapheresis. Lymphotoxic chemotherapeutic agents (e.g., cyclophosphamide, ifosfamide, bendamustine) within 2 weeks of leukapheresis. Experimental agents within 4 weeks of leukapheresis unless no response or disease progression is documented on the experimental therapy and at least 3 half-lives have elapsed prior to leukapheresis Immunosuppressive therapies within 4 weeks of leukapheresis and JCAR017 administration (e.g., calcineurin inhibitors, methotrexate or other chemotherapeutics, mycophenolyate, rapamycin, thalidomide, immunosuppressive antibodies such as anti-TNF, anti IL6, or anti-IL6R) Donor lymphocyte infusions (DLI) within 6 weeks of JCAR017 administration Radiation within 6 weeks of 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 PET-positive lesions are present, is allowed up to 2 weeks prior to leukapheresis. Allo-HSCT within 90 days of leukapheresis Prior CAR T-cell or other genetically-modified T-cell therapy, with the exception of prior JCAR017 treatment in this protocol for subjects receiving retreatment Progressive vascular tumor invasion, thrombosis, or embolism Venous thrombosis or embolism not managed on a stable regimen of anticoagulation

---

CONTACTS AND LOCATIONS

Contacts

Contact: BMS Study Connect Contact Center www.BMSStudyConnect.com 855-907-3286 Clinical.Trials@bms.com
Contact: First line of the email MUST contain the NCT# and Site #.

Locations

United States, Alabama	University of Alabama-Birmingham	Birmingham
United States, California	City of Hope	Duarte
United States, California	University of California San Francisco	San Francisco
United States, Colorado	University of Colorado	Aurora
United States, Georgia	Blood Marrow Transfer Group of Georgia - Northside Hospital	Atlanta
United States, Illinois	Northwestern University	Chicago
United States, Massachusetts	Local Institution - 0005	Boston
United States, Massachusetts	Massachusetts General Hospital	Boston
United States, Massachusetts	Beth Israel Deaconess Medical Center	Boston
United States, Nebraska	University of Nebraska Medical Center	Omaha
United States, New York	Memorial Sloan Kettering Cancer Center	New York
United States, North Carolina	Levine Cancer Institute	Charlotte
United States, Pennsylvania	UPMC Hillman Cancer Center	Pittsburgh
United States, Texas	MD Anderson Cancer Center	Houston
United States, Washington	Fred Hutchinson/University of Washington Cancer Consortium	Seattle

Sponsors and Collaborators

Juno Therapeutics, a Subsidiary of Celgene

Investigator

Study Director : Bristol-Myers Squibb Bristol-Myers Squibb

MORE INFORMATION

Other Publications

Cartron G, Fox CP, Liu FF, Kostic A, Hasskarl J, Li D, Bonner A, Zhang Y, Maloney DG, Kuruvilla J. Matching-adjusted indirect treatment comparison of chimeric antigen receptor T-cell therapies for third-line or later treatment of relapsed or refractory large B-cell lymphoma: lisocabtagene maraleucel versus tisagenlecleucel. Exp Hematol Oncol. 2022 Mar 25;11(1):17. doi: 10.1186/s40164-022-00268-z.

Ogasawara K, Lymp J, Mack T, Dell'Aringa J, Huang CP, Smith J, Peiser L, Kostic A. In Vivo Cellular Expansion of Lisocabtagene Maraleucel and Association With Efficacy and Safety in Relapsed/Refractory Large B-Cell Lymphoma. Clin Pharmacol Ther. 2022 Jul;112(1):81-89. doi: 10.1002/cpt.2561. Epub 2022 Mar 20.

Ernst M, Oeser A, Besiroglu B, Caro-Valenzuela J, Abd El Aziz M, Monsef I, Borchmann P, Estcourt LJ, Skoetz N, Goldkuhle M. Chimeric antigen receptor (CAR) T-cell therapy for people with relapsed or refractory diffuse large B-cell lymphoma. Cochrane Database Syst Rev. 2021 Sep 13;9:CD013365. doi: 10.1002/14651858.CD013365.pub2. Review.

Maloney DG, Kuruvilla J, Liu FF, Kostic A, Kim Y, Bonner A, Zhang Y, Fox CP, Cartron G. Matching-adjusted indirect treatment comparison of liso-cel versus axi-cel in relapsed or refractory large B cell lymphoma. J Hematol Oncol. 2021 Sep 8;14(1):140. doi: 10.1186/s13045-021-01144-9.

Westin JR, Kersten MJ, Salles G, Abramson JS, Schuster SJ, Locke FL, Andreadis C. Efficacy and safety of CD19-directed CAR-T cell therapies in patients with relapsed/refractory aggressive B-cell lymphomas: Observations from the JULIET, ZUMA-1, and TRANSCEND trials. Am J Hematol. 2021 Oct 1;96(10):1295-1312. doi: 10.1002/ajh.26301. Epub 2021 Aug 13. Review.

Ogasawara K, Dodds M, Mack T, Lymp J, Dell'Aringa J, Smith J. Population Cellular Kinetics of Lisocabtagene Maraleucel, an Autologous CD19-Directed Chimeric Antigen Receptor T-Cell Product, in Patients with Relapsed/Refractory Large B-Cell Lymphoma. Clin Pharmacokinet. 2021 Dec;60(12):1621-1633. doi: 10.1007/s40262-021-01039-5. Epub 2021 Jun 14. Erratum in: Clin Pharmacokinet. 2021 Jul 3;:.

Salles G, Spin P, Liu FF, Garcia J, Kim Y, Hasskarl J. Indirect Treatment Comparison of Liso-Cel vs. Salvage Chemotherapy in Diffuse Large B-Cell Lymphoma: TRANSCEND vs. SCHOLAR-1. Adv Ther. 2021 Jun;38(6):3266-3280. doi: 10.1007/s12325-021-01756-0. Epub 2021 May 10.

Patrick DL, Powers A, Jun MP, Kim Y, Garcia J, Dehner C, Maloney DG. Effect of lisocabtagene maraleucel on HRQoL and symptom severity in relapsed/refractory large B-cell lymphoma. Blood Adv. 2021 Apr 27;5(8):2245-2255. doi: 10.1182/bloodadvances.2020003503.

Abramson JS, Siddiqi T, Garcia J, Dehner C, Kim Y, Nguyen A, Snyder S, McGarvey N, Gitlin M, Pelletier C, Jun MP. Cytokine release syndrome and neurological event costs in lisocabtagene maraleucel-treated patients in the TRANSCEND NHL 001 trial. Blood Adv. 2021 Mar 23;5(6):1695-1705. doi: 10.1182/bloodadvances.2020003531.

Abramson JS, Palomba ML, Gordon LI, Lunning MA, Wang M, Arnason J, Mehta A, Purev E, Maloney DG, Andreadis C, Sehgal A, Solomon SR, Ghosh N, Albertson TM, Garcia J, Kostic A, Mallaney M, Ogasawara K, Newhall K, Kim Y, Li D, Siddiqi T. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. Lancet. 2020 Sep 19;396(10254):839-852. doi: 10.1016/S0140-6736(20)31366-0. Epub 2020 Sep 1.

Responsible Party : Juno Therapeutics, a Subsidiary of Celgene

ClinicalTrials.gov Identifier : NCT02631044

Other Study ID Numbers : 017001

First Posted : December 15, 2015

Last Update Posted : August 2, 2022

Last Verified : July 2022

Individual Participant Data (IPD) Sharing Statement:	
Plan to Share IPD:	Undecided
Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
Keywords provided by Juno Therapeutics, a Subsidiary of Celgene:	*CAR* *JCAR017* *chimeric antigen receptor* *non-Hodgkin lymphoma CAR T cells* *autologous T cell therapy* *cell therapy* *NHL*
Additional relevant MeSH terms :	*Lymphoma* *Lymphoma, Non-Hodgkin* *Lymphoma, B-Cell* *Lymphoma, Mantle-Cell* *Lymphoma, Large B-Cell, Diffuse* *Neoplasms by Histologic Type* *Neoplasms* *Lymphoproliferative Disorders* *Lymphatic Diseases* *Immunoproliferative Disorders* *Immune System Diseases*