Study Evaluating the Safety and Efficacy of JCARH125 in Subjects With Relapsed and/or Refractory Multiple Myeloma

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT03430011	RECRUITING	FEBRUARY 12, 2018	AUGUST 11, 2020

STUDY DESCRIPTION

Brief Summary

This is an open-label, multicenter, Phase 1/2 study to determine the safety and efficacy of JCARH125, a CAR T-cell product that targets B-cell maturation antigen (BCMA), in adult subjects with relapsed and/or refractory multiple myeloma. The study will include a Phase 1 part to determine the recommended dose of JCARH125 in subjects with relapsed and/or refractory multiple myeloma, followed by a Phase 2 part to further evaluate the safety and efficacy of JCARH125 at the recommended dose. The safety and tolerability of JCARH125 in subjects who receive prophylactic treatment with anakinra will be evaluated in a separate Phase 1 cohort. The antitumor activity of JCARH125 in subjects who have been previously treated with BCMA-directed therapy will be evaluated in separate Phase 2a cohorts.

Condition or Disease: Multiple Myeloma

Intervention/treatment: Biological: JCARH125
Biological: JCARH125 + anakinra

Phase: Phase 1/Phase 2

DETAILED DESCRIPTION

N/A

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 245 participants

Intervention Model : Single Group Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: Protocol H125001: An Open-Label Phase 1/2 Study of JCARH125, BCMA-targeted Chimeric Antigen Receptor (CAR) T Cells, in Subjects With Relapsed or Refractory Multiple Myeloma

Actual Study Start Date: February 2018

Estimated Primary Completion Date: January 2022

Estimated Study Completion Date: June 2023

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: JCARH125 Subjects will receive a course of lymphodepleting chemotherapy with fludarabine and cyclophosphamide followed by a single dose of JCARH125	Biological: JCARH125 Participants will undergo leukapheresis to isolate peripheral blood mononuclear cells (PBMCs) for the production of JCARH125. During JCARH125 production, participants may receive bridging chemotherapy for disease control. Following successful generation of JCARH125 product, participants will receive a course of lymphodepleting chemotherapy followed by one dose of JCARH125 administered intravenously (IV).
Experimental: JCARH125 + anakinra Subjects will receive a course of lymphodepleting chemotherapy with fludarabine and cyclophosphamide followed by prophylactic treatment with anakinra and a single dose of JCARH125	Biological: JCARH125 + anakinra Participants will undergo leukapheresis to isolate PBMCs for the production of JCARH125. During JCARH125 production, participants may receive bridging chemotherapy for disease control. Following successful generation of JCARH125 product, participants will receive a course of lymphodepleting chemotherapy followed by two doses of anakinra administered subcutaneously and one dose of JCARH125 administered IV. Subjects receive anakinra for 5 consecutive days following JCARH125 infusion.

OUTCOME MEASURES

Primary Outcome Measures: 1. Phase 1: Incidence and severity of adverse events [Time Frame: 2 years]
Proportion of subjects with adverse events overall and by severity grade
2. Phase 1: Incidence of dose-limiting toxicities (DLTs) [Time Frame: 21 days]
Proportion of subjects with adverse events meeting DLT criteria
3. Phase 1: Incidence and severity of clinically significant laboratory abnormalities [Time Frame: 2 years]
Proportion of subjects with clinically significant laboratory abnormalities overall and by severity grade
4. Phase 1 Anakinra Cohort only: Incidence and severity of Grade 2 or higher cytokine release syndrome (CRS) [Time Frame: 2 years]
Proportion of subjects with Grade 2 or higher CRS
5. Phase 1 Anakinra Cohort only: Percentage of subjects with no CRS on Days 1, 2, or 3 following JCARH125 infusion [Time Frame: 2 years]
Proportion of subjects with no CRS on Days 1, 2, or 3 following JCARH125 infusion
6. Phase 1 Anakinra Cohort only: Time to onset of Grade 2 or higher CRS [Time Frame: 2 years]
Median time to onset of Grade 2 or higher CRS

Secondary Outcome Measures:	7. Phase 2: Overall response rate [Time Frame: 2 years] Proportion of subjects with a partial response or better by International Myeloma Working Group (IMWG) criteria 1. Phase 1 and Phase 2: Maximum concentration (Cmax) of JCARH125 in the blood [Time Frame: 2 years] 2. Phase 1 and Phase 2: Time to maximum concentration (Tmax) of JCARH125 in the blood [Time Frame: 2 years] 3. Phase 1 and Phase 2: Area under the concentration vs time curve (AUC) of JCARH125 in the blood [Time Frame: 2 years] 4. Phase 1 and Phase 2: Duration of persistence of JCARH125 CAR T cells in the blood [Time Frame: 2 years] 5. Phase 1: Overall response rate [Time Frame: 2 years] Proportion of subjects with a partial response (PR) or better by IMWG criteria 6. Phase 1 and Phase 2: Complete response (CR) rate [Time Frame: 2 years] Proportion of subjects with a CR by IMWG criteria 7. Phase 2: Duration of response [Time Frame: 2 years] Time from first response (stringent complete response [sCR], CR, very good partial response [VGPR], or PR) to the earlier date of progressive disease (PD) or death due to any cause 8. Phase 2: Duration of CR [Time Frame: 2 years] Time from first sCR or CR to the earlier date of PD or death due to any cause 9. Phase 2: incidence and severity of adverse events [Time Frame: 2 years] Proportion of subjects with adverse events overall and by severity grade 10. Phase 2: Incidence and severity of clinically significant laboratory abnormalities [Time Frame: 2 years] Proportion of subjects with clinically significant laboratory abnormalities overall and by severity grade 11. Phase 2: Overall survival [Time Frame: 2 years] Time from JCARH125 infusion until death 12. Phase 2: Progression-free survival [Time Frame: 2 years] Time from JCARH125 infusion until the earliest of date of death or disease progression as assessed by IMWG criteria 13. Phase 2: Time to response [Time Frame: 2 years] Time from JCARH125 infusion to first documentation of PR or better 14. Phase 2: Time to CR [Time Frame: 2 years] Time from JCARH125 infusion to first documentation of CR or better 15. Phase 2 (excluding Phase 2a): Changes in measures of health-related quality of life (HRQoL) [Time Frame: 2 years] Change from baseline in HRQoL 16. Phase 2 (excluding Phase 2a): Numbers of days in the intensive care unit (ICU) [Time Frame: 2 years] 17. Phase 2 (excluding Phase 2a): Number of non-ICU inpatient days [Time Frame: 2 years]

ELIGIBILITY CRITERIA

Ages Eligible for Study:	18 Years and older (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Key Inclusion Criteria:
1. Diagnosis of multiple myeloma (MM) with relapsed and/or refractory (R/R) disease. Participants must have received at least 3 prior anti-myeloma treatment regimens. Participants must have previously received all of the following therapies and must be refractory to the last line of therapy prior to entering the study (not applicable to Phase 2a):
1. Autologous stem cell transplant
2. A regimen that included an immunomodulatory agent (eg, thalidomide, lenalidomide, pomalidomide) and a proteasome inhibitor (eg, bortezomib, carfilzomib, ixazomib), either alone or in combination
3. Anti-CD38 (eg, daratumumab) as part of a combination regimen or as a monotherapy
Subjects who have received prior allogeneic stem cell transplant or donor lymphocyte infusion at least 100 days before enrollment with no signs of acute or chronic graft-versus-host disease (GVHD) will be considered eligible. Subjects who were not candidates to receive one or more of the above treatments (ie, contraindicated) are eligible.
2. Subjects must have measurable disease.
3. Subject must be willing to provide fresh bone marrow biopsy samples during Screening (and prior to study treatment, if required).
4. Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1
5. Adequate renal, bone marrow, hepatic, pulmonary, and cardiac function
6. Phase 2a cohorts only - Subjects with R/R MM who have been previously treated with prior BCMA-directed anti-myeloma therapy, achieved at least a partial response (PR) and progressed on the following treatment:
1. Subjects who have received prior BCMA-directed CAR T-cell therapy. The last CAR T-cell therapy must have been received at least 6 months prior to JCARH125 screening.
2. Subjects who have received prior BCMA-directed T-cell engager therapy.
3. Subjects who have received prior BCMA-directed antibody-drug conjugate therapy.
Exclusion Criteria:
1. Subjects with known active or history of CNS involvement by malignancy
2. Subjects with solitary plasmacytoma; active or history of plasma cell leukemia (PCL); Waldenstrom's macroglobulinemia; Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal plasmaproliferative disorder, Skin changes (POEMS) syndrome; or symptomatic amyloidosis
3. Subjects who are considered eligible to receive and have not refused an autologous stem cell transplant
4. History of another primary malignancy that has not been in remission for at least 3 years. The following are exempt from the 3-year limit: non-melanoma skin cancer, 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.
5. Require systemic immunosuppressive therapies (eg, calcineurin inhibitors, methotrexate, mycophenolate, rapamycin, thalidomide, immunosuppressive antibodies such as anti-IL-6 or anti-IL-6 receptor [IL-6R])
6. Prior CAR T-cell or other genetically-modified T-cell therapy (not applicable for subjects enrolled in Phase 2a cohorts)
7. Prior treatment with a BCMA-targeted agent (not applicable for subjects enrolled in Phase 2a cohorts)
8. 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
9. Untreated or active infection at time of initial screening, at the time of leukapheresis, within 72 hrs before lymphodepletion, or 5 days before JCARH125 infusion.
10. History of any of the following cardiovascular conditions within 6 months of screening: Class III or IV heart failure as defined by the New York Heart Association (NYHA), myocardial infarction, unstable angina, uncontrolled or symptomatic atrial arrhythmias, any ventricular arrhythmias, or other clinically significant cardiac disease
11. Subjects with known hypersensitivity to E Coli-derived proteins (only applicable to subjects in Phase 1 Anakinra Cohort)
12. History of severe immediate hypersensitivity reaction to any of the protocol-mandated or recommended agents used in this study

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CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

United States, Alabama	University of Alabama	Birmingham
United States, California	City of Hope Comprehensive Cancer Center	Duarte
United States, California	University of California, Los Angeles	Los Angeles
United States, California	University of California	San Francisco
United States, Colorado	SCRI - Colorado Blood Cancer Institute	Denver
United States, Georgia	Winship Cancer Institute at Emory University	Atlanta
United States, Illinois	The University of Chicago Medicine	Chicago
United States, Kansas	Kansas University Medical Center	Westwood
United States, Maryland	Johns Hopkins Hospital	Baltimore
United States, Massachusetts	Massachusetts General Hospital	Boston
United States, Michigan	Karmanos Cancer Institute Wayne State	Detroit
United States, Minnesota	Mayo Clinic	Rochester
United States, New Jersey	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, Oregon	Oregon Health & Science University	Portland

United States, Texas	SCRI - Texas	San Antonio
United States, Washington	Swedish Cancer Institute	Seattle
United States, Washington	Fred Hutchinson Cancer Research Center	Seattle
United States, Wisconsin	Froedtert Hospital Medical College Wisconsin	Milwaukee

Sponsors and Collaborators

Juno Therapeutics, a Subsidiary of Celgene

Investigator

Study Director :	Mariana Cota, MD	Juno Therapeutics, Inc.

MORE INFORMATION

Responsible Party :	Juno Therapeutics, a Subsidiary of Celgene
ClinicalTrials.gov Identifier :	NCT03430011
Other Study ID Numbers :	H125001
First Posted :	February 12, 2018
Last Update Posted :	August 11, 2020
Last Verified :	August 2020
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:	*JCARH125* *multiple myeloma* *CAR T cells* *B-cell maturation antigen BCMA* *autologous T-cell therapy* *immunotherapy* *chimeric antigen receptor*
Additional relevant MeSH terms :	*Multiple Myeloma* *Neoplasms, Plasma Cell*