Study of CC-93269, a BCMA x CD3 T Cell Engaging Antibody, in Subjects With Relapsed and Refractory Multiple Myeloma

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT03486067	RECRUITING	APRIL 3, 2018	AUGUST 11, 2020

STUDY DESCRIPTION

Brief Summary

Study CC-93269-MM-001 is an open-label, Phase 1, dose escalation (Part A) and expansion (Parts B and C), first-in-human clinical study of CC-93269 in subjects with relapsed and refractory multiple myeloma.

Condition or Disease: Multiple Myeloma

Intervention/treatment: Drug: CC-93269

Phase: Phase 1

DETAILED DESCRIPTION

The dose escalation part (Part A) of the study will evaluate the safety and tolerability of escalating doses of CC-93269, administered intravenously (IV), to determine the MTD and NTD of both the first dose and subsequent doses of CC-93269. The expansion part (Part B) will further evaluate the safety and efficacy of CC-93269 administered IV at or below the MTD in selected expansion cohorts of up to approximately 20 evaluable subjects each in order to determine the RP2D. CC-93269, administered IV followed by subcutaneously (SC), will also be evaluated (Part C). One or more dosing regimens may be selected for cohort expansion. All treatments will be administered in 28-day cycles for up to 2 years until confirmed disease progression, unacceptable toxicity, or subject/Investigator decision to withdraw.

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 115 participants

Intervention Model : Single Group Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Phase 1, Open-label, Dose Finding Study of CC-93269, a BCMA X CD3 T Cell Engaging Antibody, in Subjects With Relapsed and Refractory Multiple Myeloma.

Actual Study Start Date: April 2018

Estimated Primary Completion Date: October 2023

Estimated Study Completion Date: November 2023

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: Administration of CC-93269 CC-93269 by intravenous (IV) infusion or subcutaneous (SC) injection on a 28 day cycle.	Drug: CC-93269 CC-93269

OUTCOME MEASURES

Primary Outcome Measures:
1. Adverse Events (AEs) [Time Frame: Up to 48 months]
Number of participants with Adverse Events
2. Dose Limiting Toxicity (DLT) [Time Frame: Up to 48 months]
Is defined as any of the toxicities occurring within the DLT assessment window (Cycle 1, Days 1 to 28) except those that are clearly and incontrovertibly due to extraneous causes.
3. Non-Tolerated Dose (NTD) [Time Frame: Up to 48 months]
Is defined as a dose level at which 2 or more of up to 6 evaluable subjects in any dose cohort experience a DLT in the DLT window.
4. Maximum Tolerated Dose (MTD) [Time Frame: Up to 48 months]
Is defined as the last dose cohort below the NTD with 0 or 1 out of 6 evaluable subjects experiencing a DLT during the DLT window.

Secondary Outcome Measures:
1. Pharmacokinetics - CL [Time Frame: Up to 48 months]
Apparent total body clearance
2. Pharmacokinetics - Vss [Time Frame: Up to 48 months]
Volume of distribution at steady-state
3. Overall Response Rate (ORR) [Time Frame: Up to 48 months]
Is defined as the proportion of subjects who achieve a partial response or better (eg, PR, VGPR, CR or sCR), according to International Myeloma Working Group (IMWG) response criteria.
4. Time to Response [Time Frame: Up to 48 months]
Is defined as the time from the first CC-93269 dose date to the date of first documented response (PR or better).
5. Duration of Response [Time Frame: Up to 48 months]
Is defined as the time from the earliest date of documented response (≥ PR) to the first documented disease progression or death, whichever occurs first.

6. Progression Free Survival [Time Frame: Up to 48 months]
Is defined as the time from the first dose of CC-93269 to progressive disease or death from any cause, whichever occurs first.
7. Overall Survival [Time Frame: Up to 48 months]
Is defined as the time from the first dose of CC-93269 to death from any cause.
8. Pharmacokinetics - Cmax [Time Frame: Up to 48 months]
Maximum serum concentration of drug
9. Pharmacokinetics - Cmin [Time Frame: Up to 48 months]
Minimum serum concentration of drug
10. Pharmacokinetics - AUC [Time Frame: Up to 48 months]
Area under the curve
11. Pharmacokinetics - tmax [Time Frame: Up to 48 months]
Time to peak (maximum) serum concentration
12. Pharmacokinetics - t1/2 [Time Frame: Up to 48 months]
Terminal Half-life
13. Pharmacokinetics - accumulation index of CC-93269 [Time Frame: Up to 48 months]
Accumulation ratio of drug
14. Presence and frequency of anti-drug antibodies (ADA) [Time Frame: Up to 48 months]
Detection of anti-drug antibodies in participants and frequency of anti-drug antibodies
15. Evaluate measures of tumor sensitivity/ resistance to CC-93269 [Time Frame: Up to 48 months]
Measurement of tumor and immune factors

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:
Subjects must satisfy the following criteria to be enrolled in the study:
1. Subject must understand and voluntarily sign an informed consent form (ICF) prior to any study-related assessments/procedures being conducted.
2. Subject (male or female) is ≥ 18 years of age the time of signing the ICF.
3. Subject has a history of Multiple Myeloma (MM) with relapsed and refractory disease, and must have failed treatment with, are intolerant to or are not candidates for available therapies that are known to confer clinical benefit to patients with relapsed and refractory MM.
4. Subjects must have measurable disease (as determined by the central lab).
5. Subject consents to hospitalization for monitoring and collection of study peripheral blood samples.
6. Subject consents to serial bone marrow aspirations and/or biopsies during Screening, study treatment and at the end of treatment.
7. Subject has an Eastern Cooperative Oncology Group (ECOG) PS of 0 or 1.
8. Subjects must have adequate hematologic, liver, renal, and coagulation function as assessed by laboratory tests.
9. Females and males must practice true abstinence or agree to contraceptive methods throughout the study, and during the safety follow-up period.
Exclusion Criteria:
The presence of any of the following will exclude a subject from enrollment:
1. Unless otherwise specified, Subject has received prior investigational therapy directed at B cell maturation antigen (BCMA). In selected cohort(s) of Parts A and B, prior therapy directed at BCMA may be required for enrollment
2. Subject has symptomatic central nervous system involvement of multiple myeloma.
3. Subject has non-secretory multiple myeloma, plasma cell leukemia, Waldenstrom's macroglobulinemia, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes), or amyloidosis.
4. Subject is on chronic systemic immunosuppressive therapy or corticosteroids.
5. Subjects with clinically significant cardiac disease.
6. Subject had a prior autologous stem cell transplant ≤ 3 month prior to starting CC-93269.
7. Subject had a prior allogeneic stem cell transplant ≤ 12 month prior to starting CC-93269.
8. Subject had a prior systemic cancer-directed treatments or investigational modalities ≤ 5 half-lives or 4 weeks prior to starting CC-93269, whichever is shorter. Subjects must have recovered from any clinically significant non-hematologic toxicities (ie, to Grade ≤1) of prior systemic anti-cancer directed treatments unless otherwise specified
9. Subject had major surgery ≤ 2 weeks prior to starting CC-93269.
10. Subject is a pregnant or lactating female.
11. Subject has known history or serologic evidence of human immunodeficiency virus (HIV) infection.
12. Subject has known history, virologic or serological evidence of hepatitis B or C virus (HBV/HCV) infection. Subjects who had HCV but have received an antiviral treatment and show no detectable HCV viral RNA for 6 months are eligible
13. Subject has a history of a venous thromboembolic event (VTE) within 6 months prior to study entry (eg, deep-vein thrombosis or pulmonary embolism). Subjects with distant history of VTE (ie, occurring > 6 months prior to study entry) who require ongoing treatment with chronic, therapeutic dosing of anti-coagulants (eg, warfarin, low molecular weight heparin, Factor Xa inhibitors) are eligible for study entry.
14. Subject has a history of concurrent second cancers requiring active, ongoing systemic treatment.
15. Subject has a history or presence of clinically relevant central nervous system (CNS) pathology.
16. Subject has any significant medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from participating in the study.
17. Subject has any condition (eg, active or uncontrolled infection) including the presence of laboratory abnormalities, which places the subject at unacceptable risk if he/she were to participate in the study. .
18. Subject has any condition that confounds the ability to interpret data from the study.
19. Inadequate pulmonary function.
20. Subject has active, uncontrolled, or suspected infection.

CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

United States, Alabama	University of Alabama at Birmingham	Birmingham
United States, California	UCSF Medical Center	San Francisco
United States, Connecticut	Yale Cancer Center	New Haven
United States, Georgia	Winship Cancer Institute of Emory University	Atlanta
United States, Michigan	Henry Ford Medical Center - New Center One	Detroit
United States, Washington	Swedish Cancer Institute	Seattle
Germany	Universitatsklinikum Heidelberg Medizinische Klinik Krehl-Klinik Haematologie, Onkologie, Rheumato	Heidelberg
Germany	University of Tubingen	Tübingen
Spain	Clinica Universitaria de Navarra	Pamplona
Spain	Hospital Universitario de Salamanca	Salamanca
Spain	Hospital Universtario Marques de Valdecilla	Santander
Spain	Hospital Universitario Doctor Peset	Valencia
Sweden	Skanes Universitetssjukhus Lund	Lund

Sponsors and Collaborators

Celgene

Investigator

Study Director :	Michael R Burgess, MD, PhD	Celgene

MORE INFORMATION

Responsible Party :	Celgene
ClinicalTrials.gov Identifier :	NCT03486067
Other Study ID Numbers :	CC-93269-MM-001, U1111-1210-6325, 2017-003448-19
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Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
Keywords provided by Celgene:	*Multiple Myeloma* *BCMA X CD3 T Cell* *Antibody CC-93269* *Relapsed and Refractory*
Additional relevant MeSH terms :	*Multiple Myeloma* *Neoplasms, Plasma Cell*