A Study of CC-99712, a BCMA Antibody-Drug Conjugate, in Subjects With Relapsed and Refractory Multiple Myeloma

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT04036461	RECRUITING	JULY 29, 2019	AUGUST 31, 2020

STUDY DESCRIPTION

Brief Summary

Study CC-99712-MM-001 is an open-label, Phase 1, dose escalation (Part A) and expansion (Part B), First-in-Human (FIH) clinical study of CC-99712 in subjects with relapsed and refractory multiple myeloma (MM). The dose escalation part (Part A) of the study will evaluate the safety and tolerability of escalating doses of CC-99712, administered intravenously (IV), to determine the maximum tolerated dose (MTD) and non-tolerated dose (NTD) of CC-99712 using a modified accelerated titration design and Bayesian methodology. The MTD and NTD may be established separately for CC-99712 administered at Q3W and/ or Q4W schedules. The expansion part (Part B) will further evaluate the safety and efficacy of CC-99712 administered at or below the MTD in selected expansion cohorts in order to determine the RP2D. One or more dosing regimens may be selected for cohort expansion. All subjects will be treated until confirmed disease progression per IMWG criteria, unacceptable toxicity, or subject/Investigator decision to withdraw.

Condition or Disease: Multiple Myeloma

Intervention/treatment: Drug: CC-99712

Phase: Phase 1

DETAILED DESCRIPTION

N/A

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 120 participants

Intervention Model : Single Group Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Phase 1, Multicenter, Open-label, Dose Finding Study of CC-99712, a BCMA Antibody-Drug Conjugate, in Subjects With Relapsed and Refractory Multiple Myeloma

Actual Study Start Date: August 2019

Estimated Primary Completion Date: November 2024

Estimated Study Completion Date: November 2024

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: Administration of CC-99712 CC-99712 will be administered via intravenous (IV) infusion once per 21-days on a Once every three weeks (Q3W) schedule, and once per 28-days on a Once every four weeks (Q4W) schedule	Drug: CC-99712 CC-99712

OUTCOME MEASURES

Primary Outcome Measures:
1. Adverse Events (AEs) [Time Frame: From enrollment until at least 42 days after completion of study treatment]
Number of subjects with adverse event
2. Non-Tolerated Dose (NTD) in subjects with relapsed and refractory MM [Time Frame: Up to 28 days]
Is defined as the dose that causes DLTs in more than 33% of patient population during the first cycle of treatment.
3. Maximum Tolerated Dose (MTD) in subjects with relapsed and refractory MM [Time Frame: Up to 28 days]
Is defined as the highest dose that causes DLTs in no more than 33% of patient population during the first cycle of treatment.
4. Dose Limiting Toxicity (DLT) in subjects with relapsed and refractory MM [Time Frame: Up to 28 days]
Is defined as any of the following toxicities occurring within the DLT assessment window

Secondary Outcome Measures:
1. Overall Response Rate (ORR) [Time Frame: Up to 3 years]
Is defined as the proportion of subjects who achieve a partial response or better (eg, Partial response (PR), Very good partial response (VGPR), Complete response (CR) or sCR), according to IMWG response criteria.
2. Time to Response [Time Frame: Up to 3 years]
Is defined as the time from the first CC-99712 dose date to the date of first documented response (PR or better).
3. Duration of Response [Time Frame: Up to 3 years]
Is defined as the time from the earliest date of documented response (≥ PR) to the first documented disease progression or death, whichever occurs first.
4. Progression-free Survival (PFS) [Time Frame: Up to 3 years]
Is defined as the time from the first dose of CC-99712 to progressive disease (PD) or death from any cause, whichever occurs first.
5. Overall Survival (OS) [Time Frame: Up to 3 years]
Is defined as the time from the first dose of CC-99712 to death from any cause.
6. Pharmacokinetics- Cmax [Time Frame: Up to 3 years]
Maximum plasma concentration of drug

7. Pharmacokinetics- Cmin [Time Frame: Up to 3 years]
Minimum plasma concentration of drug
8. Pharmacokinetics- AUC [Time Frame: Up to 3 years]
Area under the curve
9. Pharmacokinetics- tmax [Time Frame: Up to 3 years]
Time to peak (maximum) serum concentration
10. Pharmacokinetics- t1/2 [Time Frame: Up to 3 years]
Half-life
11. Pharmacokinetics- CL [Time Frame: Up to 3 years]
Clearance
12. Pharmacokinetics- Vss [Time Frame: Up to 3 years]
Volume of Distribution
13. Presence and frequency of ADA using a validated bridging immunoassay with electrochemiluminescence detection [Time Frame: Up to 3 years]
Anti-CC-99712 antibodies

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 (male or female) is ≥ 18 years of age at the time of signing the ICF.
2. Subject has a history of MM with relapsed and refractory disease, and must:
- Have disease that is nonresponsive while on their last antimyeloma therapy or documented disease progression on or within 60 days from the last dose of their last antimyeloma therapy; and,
- Must have received at least 3 prior MM treatment regimens. and,
- Must have received a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody (eg, daratumumab); and,
- Should have failed treatment with or are intolerant to all established therapies.
3. Subjects must have measurable disease, including at least one of the criteria below:
- M-protein quantities ≥ 0.5 g/dL by sPEP or
- ≥ 200 mg/24 hours urine collection by uPEP or
- Serum FLC levels > 100 mg/L (milligrams/liter involved light chain) and an abnormal kappa/lambda (κ/λ) ratio in patients without detectable serum or urine M-protein or
- For subjects with immunoglobulin class A (IgA) myeloma whose disease can only be reliably measured by quantitative immunoglobulin measurement, a serum IgA level ≥ 0.50 g/dL.
4. Subject has an ECOG PS of 0-1.
5. Subjects must have the following laboratory values (determined by local laboratory):
- Absolute neutrophil count (ANC) ≥ 1.0 x 10^9/L
- Platelets (plt) ≥ 75 x 10^9/L.
- Potassium within normal limits or correctable with supplements.
- Aspartate aminotransferase (AST/SGOT) and alanine aminotransferase (ALT/SGPT) ≤ 2.5 x upper limit of normal (ULN).
- Serum bilirubin ≤ 1.5 x ULN (or ≤ 2.0 x ULN for subjects with documented Gilbert's syndrome).
- Estimated serum creatinine clearance of ≥ 60 mL/min
- International normalized ratio (INR) < 1.5 x ULN and partial thromboplastin time (PTT) < 1.5 x ULN. 6. Females of childbearing potential (FCBP) must: - Either commit to true abstinence from heterosexual contact (which must be reviewed on a monthly basis and source documented) or agree to use, and be able to comply with, at least two effective contraceptive methods (oral, injectable, or implantable hormonal contraceptive; tubal ligation; intra-uterine device; barrier contraceptive with spermicide; or vasectomized partner), one of which must be barrier, from signing the ICF, throughout the study, during dose interruptions, and for up to 42 days following the last dose of CC-99712; and - Have two negative pregnancy tests as verified by the Investigator prior to starting CC-99712. Subject must agree to ongoing pregnancy testing during the course of the study, and after end of study treatment. This applies even if the subject practices true abstinence from heterosexual contact. The subject may not receive IP until the Investigator has verified that the result of the pregnancy test is negative. - a negative serum pregnancy test (sensitivity of at least 25 mIU/mL) at Screening - a negative serum or urine pregnancy test (Investigator's discretion) within 72 hours prior to Cycle 1 Day -1 of study treatment, and within 72 hours prior to Day -1 of every subsequent cycle (note that the Screening serum pregnancy test can be used as the test prior to Day -1 study treatment if it is performed within the prior 72 hours). A serum or urine pregnancy test (investigators discretion) must also be performed at the end of study for each FCBP. - Avoid conceiving for 42 days after the last dose of CC-99712.7. Males must practice true abstinence (which must be reviewed on a monthly basis) or agree to use a condom (a latex condom is recommended) during sexual contact with a pregnant female or a FCBP and will avoid conceiving from signing the ICF, while participating in the study, during dose interruptions, and for at least 42 days following CC-99712 discontinuation, even if he has undergone a successful vasectomy. 8. Subject is willing and able to adhere to the study visit schedule and other protocol requirements. Exclusion Criteria: The presence of any of the following will exclude a subject from enrollment: 1. In Part A only, subject has received prior investigational therapy directed at BCMA. 2. Subject has symptomatic central nervous system involvement of MM. 3. Subject has nonsecretory MM, plasma cell leukemia, Waldenstrom's macroglobulinemia, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes), or amyloidosis. 4. Subjects with a history of class III or IV congestive heart failure (CHF) or severe non-ischemic cardiomyopathy, unstable angina, myocardial infarction, or ventricular arrhythmia within the previous 6 months prior to signing ICF. 5. Subject had a prior autologous stem cell transplant ≤ 3 months prior to starting CC-99712. 6. Subject had a prior allogeneic stem cell transplant with either standard or reduced intensity conditioning ≤ 6 months prior to starting CC-99712 or is on systemic immunosuppression for graft-versus host disease. 7. Subject had a prior chimeric antigen receptor T (CAR T) cell product ≤ 4 weeks prior to starting CC-99712. 8. Subject had a prior systemic cancer-directed treatments or investigational modalities within 5 pharmacokinetic half-lives or 2 weeks prior to starting CC-99712, whichever is longer. The only exception is emergency use of a short course of corticosteroids (equivalent of dexamethasone 40 mg/day for a maximum 4 days) before treatment. 9. Subject had major surgery ≤ 2 weeks prior to starting CC-99712. Subjects must have recovered from any clinically significant effects of recent surgery. 10. Subject is a pregnant or lactating female. 11. Subject has known human immunodeficiency virus (HIV) infection. 12. Subject has known history of chronic, active hepatitis B or C virus (HBV/HCV) infection. 13. Subject requires ongoing treatment with chronic, therapeutic dosing of anti-coagulants (eg, warfarin, low molecular weight heparin, Factor Xa inhibitors). 14. Subject has a history of concurrent second cancers requiring active, ongoing systemic treatment. 15. Subject has known history of cirrhosis or has clinically significant liver or biliary disease. Subjects with stable chronic liver or biliary disease (such as Gilbert's syndrome, asymptomatic gallstones, or hepatobiliary involvement of malignancy) may participate in the study, however, sponsor medical monitor must be contacted for a discussion before enrollment. 16. Subject has a history of clinically significant corneal disease requiring therapy or ongoing active corneal disease. 17. Subject has active peripheral neuropathy or neuropathic pain Grade 2 or higher, as defined by the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE v5.0).

CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

United States, California	University of California San Diego Moores Cancer Center	La Jolla
United States, Florida	Florida Cancer Specialists	Sarasota
United States, New York	Roswell Park Cancer Institute	Buffalo
United States, New York	Mount Sinai Hospital	New York
United States, Oregon	Oregon Health & Science University	Portland
United States, Texas	UT Southwestern Medical Center	Dallas
United States, Washington	Swedish Medical Center	Seattle
Canada, Alberta	Tom Baker Cancer Center	Calgary

Canada, Ontario	Princess Margaret Cancer Centre	Toronto
Canada, Quebec	Hopital Maisonneuve Rosemont dba CIUSSS de lEst de Ile de Montreal	Montreal

Sponsors and Collaborators

Celgene

Investigator

Study Director :	Kaida Wu, MD, PhD	Translational Development.

MORE INFORMATION

Responsible Party :	Celgene
ClinicalTrials.gov Identifier :	NCT04036461
Other Study ID Numbers :	CC-99712-MM-001, U1111-1231-9404
First Posted :	July 29, 2019
Last Update Posted :	August 31, 2020
Last Verified :	August 2020
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:	*Relapsed and refractory* *CC-99712* *BCMA Antibody drug conjugate* *Multiple Myeloma*
Additional relevant MeSH terms :	*Multiple Myeloma* *Neoplasms, Plasma Cell*