Efficacy and Safety Study of bb2121 in Subjects With Relapsed and Refractory Multiple Myeloma

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT03361748	ACTIVE, NOT RECRUITING	DECEMBER 5, 2017	JUNE 16, 2020

STUDY DESCRIPTION

Brief Summary

This is an open label, single-arm, multicenter, Phase 2 study to evaluate the efficacy and safety of bb2121 in subjects with relapsed and refractory multiple myeloma. A leukapheresis procedure will be performed to manufacture bb2121 chimeric antigen receptor (CAR) modified T cells. Prior to bb2121 infusion subjects will receive lymphodepleting therapy with fludarabine and cyclophosphamide.

Condition or Disease: Multiple Myeloma

Intervention/treatment: Biological: bb2121

Phase: Phase 2

DETAILED DESCRIPTION

Anti-myeloma bridging treatment is allowed for disease control while bb2121 is being manufactured.
Three sites in Japan will be activated in 2019 and will be open for enrollment to patients in Japan.

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 149 participants

Intervention Model : Single Group Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Phase 2, Multicenter Study to Determine the Efficacy and Safety of bb2121 in Subjects With Relapsed and Refractory Multiple Myeloma

Actual Study Start Date: December 2017

Estimated Primary Completion Date: November 2024

Estimated Study Completion Date: November 2024

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: Administration of bb2121 bb2121 autologous CAR T cells will be infused at a dose ranging from 15 - 45 x 10^7 CAR+ T cells after receiving lymphodepleting chemotherapy.	Biological: bb2121 : bb2121 consists of autologous T lymphocytes transduced with an anti-BCMA02 CAR lentiviral vector to express a chimeric antigen receptor targeting the human B cell maturation antigen (anti-BCMA CAR).

OUTCOME MEASURES

Primary Outcome Measures:
1. Overall Response Rate (ORR) [Time Frame: Minimum of 24 months post-bb2121 infusion]
Percentage of subjects who achieved partial response (PR) or better according to IMWG Uniform Response Criteria for Multiple Myeloma.

Secondary Outcome Measures:
1. Pharmacokinetics - AUC [Time Frame: Minimum of 24 months post-bb2121 infusion]
Area under the curve of the transgene level
2. Immunogenicity [Time Frame: Minimum of 24 months post-bb2121 infusion]
Development of an anti-CAR antibody response
3. Minimal Residual Disease (MRD) [Time Frame: Minimum of 24 months post-bb2121 infusion]
Proportion of MRD evaluable subjects that are MRD negative
4. Complete Response (CR) Rate [Time Frame: Minimum of 24 months post-bb2121 infusion]
Percentage of subjects who achieved CR or better according to IMWG Uniform Response Criteria for Multiple Myeloma
5. Time to Response [Time Frame: Minimum of 24 months post-bb2121 infusion]
Time from first bb2121 infusion to first documentation of response
6. Duration of Response [Time Frame: Minimum of 24 months post-bb2121 infusion]
Time from first response to disease progression or death from any cause
7. Progression-free Survival (PFS) [Time Frame: Minimum of 24 months post-bb2121 infusion]
Time from first bb2121 infusion to first documentation of progressive disease (PD), or death due to any cause, whichever occurs first
8. Time to Progression (TTP) [Time Frame: Minimum of 24 months post-bb2121 infusion]
Time from first bb2121 infusion to first documentation of PD
9. Overall Survival (OS) [Time Frame: Minimum of 24 months post-bb2121 infusion]
Time from first bb2121 infusion to time of death due to any cause
10. Adverse Events (AEs) [Time Frame: Minimum of 24 months post-bb2121 infusion]
Number of participants with adverse events (AEs), severity of adverse events, adverse events of special interest (AESI), and serious adverse events (SAEs)

11. Pharmacokinetics - Cmax [Time Frame: Minimum of 24 months post-bb2121 infusion]
The maximum transgene level at Tmax
12. Pharmacokinetics - Tmax [Time Frame: Minimum of 24 months post-bb2121 infusion]
Time to peak transgene level
13. Subject-reported outcomes as measured by European Organization for Research and Treatment of Cancer Quality-of-Life questionnaire (EORTC-QLQ-C30) [Time Frame: Minimum of 24 months post-bb2121 infusion]
Questionnaire will be used as a measure of health-related quality of life
14. Subject-reported outcomes as measured by EuroQoL Group EQ-5D-5L Health Questionnaire [Time Frame: : Minimum of 24 months post-bb2121 infusion]
Is a standardized measure of health status developed by the EuroQol Group in order to provide a simple, generic measure of health for clinical and economic appraisal
15. Subject-reported outcomes as measured by EORTC-QLQ-MY20 [Time Frame: Minimum of 24 months post-bb2121 infusion]
Is a 20-item myeloma module intended for use among patients varying in disease stage and treatment modality

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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:
Eligibility is determined prior to leukapheresis. Subjects must satisfy the following criteria to be enrolled in the study:
1. Subject is ≥ 18 years of age at the time of signing the informed consent form (ICF).
2. Documented diagnosis of multiple myeloma
- Must have received at least 3 prior MM treatment regimens. Note: induction with or without hematopoietic stem cell transplant and with or without maintenance therapy is considered a single regimen.
- Must have undergone at least 2 consecutive cycles of treatment for each regimen, unless PD was the best response to the regimen.
- Must have received a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody.
- Must be refractory to the last treatment regimen.
3. Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1.
4. Subjects must have measurable disease, including at least one of the criteria below:
- Serum M-protein greater or equal to 1.0 g/dL
- Urine M-protein greater or equal to 200 mg/24 h
- Serum free light chain (FLC) assay: involved FLC level greater or equal to 10 mg/dL (100 mg/L) provided serum FLC ratio is abnormal
Exclusion Criteria:
The presence of any of the following will exclude a subject from enrollment:
1. Subjects with known central nervous system involvement with myeloma.
2. History or presence of clinically relevant central nervous system (CNS) pathology.
3. Subjects with active or history of plasma cell leukemia.
4. Subjects with solitary plasmacytomas or non-secretory myeloma without other evidence of measurable disease
5. Inadequate organ function
6. Ongoing treatment with chronic immunosuppressants
7. Previous history of an allogeneic hematopoietic stem cell transplantation or treatment with any gene therapy-based therapeutic for cancer or investigational cellular therapy for cancer or BCMA targeted therapy
8. Evidence of human immunodeficiency virus (HIV) infection.
9. Seropositive for and with evidence of active viral infection with hepatitis B virus (HBV)
10. Seropositive for and with evidence of active viral infection with hepatitis B virus (HBV) and Hepatitis C virus (HCV)
11. Subjects with a history of class III or IV congestive heart failure (CHF) or severe non-ischemic cardiomyopathy, history of stroke, unstable angina, myocardial infarction, or ventricular arrhythmia within the previous 6 months.
12. Subjects with second malignancies in addition to myeloma if the second malignancy has required therapy in the last 3 years or is not in complete remission
13. Pregnant or lactating women.
14. Subject with known hypersensitivity to any component of bb2121 productThe presence of any of the following will exclude a subject from enrollment:
1. Subjects with known central nervous system involvement with myeloma. 2. History or presence of clinically relevant central nervous system (CNS) pathology. 3. Subjects with active or history of plasma cell leukemia. 4. Subjects with solitary plasmacytomas or non-secretory myeloma without other evidence of measurable disease 5. Inadequate organ function 6. Ongoing treatment with chronic immunosuppressants 7. Previous history of an allogeneic hematopoietic stem cell transplantation or treatment with any gene therapy-based therapeutic for cancer or investigational cellular therapy for cancer or BCMA targeted therapy 8. Evidence of human immunodeficiency virus (HIV) infection. 9. Seropositive for and with evidence of active viral infection with hepatitis B virus (HBV) and Hepatitis C virus (HCV) 10. Subjects with a history of class III or IV congestive heart failure (CHF) or severe non-ischemic cardiomyopathy, history of stroke, unstable angina, myocardial infarction, or ventricular arrhythmia within the previous 6 months. 11. Subjects with second malignancies in addition to myeloma if the second malignancy has required therapy in the last 3 years or is not in complete remission 12. Pregnant or lactating women. 13 Subject with known hypersensitivity to any component of bb2121 product, cyclophosphamide, fludarabine, or tocilizumab.

CONTACTS AND LOCATIONS

Contacts

Locations

United States, California	University of California - San Francisco	San Francisco
United States, Georgia	Emory University	Atlanta
United States, Massachusetts	Dana Farber Cancer Institute	Boston
United States, Massachusetts	Massachusetts General Hospital	Boston

United States, Minnesota	Mayo Clinic	Rochester
United States, New Jersey	Hackensack University Medical Center	Hackensack
United States, New York	Mt. Sinai Medical Center	New York
United States, Tennessee	Sarah Cannon Research Institute	Nashville
United States, Texas	University of Texas Southwestern Medical Center	Dallas
Belgium, Flemish Brabant	Universitaire Ziekenhuizen Leuven	Leuven
Canada	Princess Margaret Cancer Centre	Toronto
France, Hauts-de-France	Centre Hospitalier Regional Universitaire de Lille-Hopital Calude Huriez Service des Maladies du Sang	Lille
France, Pays De La Loire	Centre Hospitalier Universitaire de Nantes - Hotel Dieu	Nantes
Germany, Baden-Württemberg	Universitatsklinikum Heidelberg Medizinische Klinik Krehl-Klinik Haematologie, Onkologie, Rheumato	Heidelberg
Germany, Baden-Württemberg	University of Tübingen	Tübingen
Germany, Bavaria	Universitatsklinikum Würzburg	Würzburg
Italy, Emilia-Romagna	Azienda Ospedaliero Universitaria Di Bologna Policlinico	Bologna
Italy	Ospedali Riuniti di Bergamo	Bergamo
Japan, Kanagawa	Tokai University Hospital	Isehara
Japan, Tochigi	Jichi Medical University Hospital	Shimotsuke
Japan, Tokyo	Japan Red Cross Medical Center	Shibuya-ku
Japan	Tokyo Women's Medical University Hospital	Shinjuku City
Spain, Barcelona	Hospital Universitari Germans Trias i Pujol Can Ruti	Badalona
Spain, Navarre	Clinica Universidad de Navarra	Pamplona

Sponsors and Collaborators

Celgene

Investigator

Study Director :	Kristen Hege	Celgene

MORE INFORMATION

Other Publications	Raje N, Berdeja J, Lin Y, Siegel D, Jagannath S, Madduri D, Liedtke M, Rosenblatt J, Maus MV, Turka A, Lam LP, Morgan RA, Friedman K, Massaro M, Wang J, Russotti G, Yang Z, Campbell T, Hege K, Petrocca F, Quigley MT, Munshi N, Kochenderfer JN. Anti-BCMA CAR T-Cell Therapy bb2121 in Relapsed or Refractory Multiple Myeloma. N Engl J Med. 2019 May 2;380(18):1726-1737. doi: 10.1056/NEJMoa1817226.
Responsible Party :	Celgene
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Other Study ID Numbers :	BB2121-MM-001, U1111-1202-5554, 2017-002245-29
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Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
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Additional relevant MeSH terms :	*Multiple Myeloma* *Neoplasms, Plasma Cell*