# An Efficacy and Safety Study of bb2121 in Subjects With Relapsed and Refractory Multiple Myeloma and in Subjects With High-Risk Multiple Myeloma

| CLINICALTRIALS.GOV IDENTIFIER | RECRUITMENT STATUS | FIRST POSTED | LAST UPDATE POSTED |
|---|---|---|---|
| NCT03601078 | RECRUITING | JULY 26, 2018 | AUGUST 28, 2020 |

## STUDY DESCRIPTION

### Brief Summary

This study is a multi-cohort, open-label, multicenter Phase 2 study to evaluate the efficacy and safety of bb2121 in subjects with relapsed and refractory MM (Cohort 1), in subjects with MM having progressed within one 18 months of initial treatment including autologous stem cell transplantation (ASCT) (Cohort 2a), and without ASCT (Cohort 2b) or, in subjects with inadequate response post ASCT during initial treatment (Cohort 2c) Approximately 181 subjects will be enrolled into one of two cohorts. Cohort 1 will enroll approximately 73 RRMM subjects with ≥ 3 prior anti-myeloma treatment regimens. Cohort 2a will enroll approximately 39 MM subjects, with 1 prior anti-myeloma therapy including ASCT and with early relapse. Cohort 2b will enroll approximately 39 MM subjects with 1 prior anti-myeloma therapy not including ASCT and with early relapse. Cohort 2c will enroll approximately 30 MM subjects with inadequate response to ASCT during their initial anti-myeloma therapy. The cohorts will start in parallel and independently.

**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 for cohorts 1, 2a and 2b only.

## STUDY DESIGN

**Study Type:** Interventional

**Estimated Enrollment :** 181 participants

**Intervention Model :** Single Group Assignment

**Masking:** None (Open Label) ()

**Primary Purpose:** Treatment

**Official Title:** A Phase 2, Multicohort, Open-label, Multicenter Study to Evaluate the Efficacy and Safety of bb2121 in Subjects With Relapsed and Refractory Multiple Myeloma and in Subjects With Clinical High-Risk Multiple Myeloma (KarMMa-2)

**Actual Study Start Date:** December 2018

**Estimated Primary Completion Date:** October 2021

**Estimated Study Completion Date:** May 2026

## ARMS AND INTERVENTIONS

| Arm | Intervention/treatment |
|---|---|
| Experimental: bb2121 in relapsed and refractory multiple myeloma patients<br>bb2121 autologous CAR T cells will be infused at a dose ranging from 150 - 450 x 10^6 CAR+ T cells after receiving lymphodepleting chemotherapy | Biological: bb2121<br>bb2121 consists of autologous T lymphocytes transduced with an anti-BCMA 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)- Cohort 1 [ Time Frame: Minimum of 2 years after bb2121 infusion ]
Percentage of subjects who achieved partial response (PR) or better according to IMWG Uniform Response Criteria for Multiple Myeloma as assessed by an independent response committee (IRC)
2. Complete response (CR) rate - Cohort 2a , b and c [ Time Frame: Minimum of 2 years after bb2121 infusion ]
Percentage of subjects who achieved CR or stringent CR according to IMWG Uniform Response Criteria for Multiple Myeloma as assessed by an IRC

Secondary Outcome Measures:
1. Complete response (CR) rate - Cohort 1 [ Time Frame: Minimum of 2 years after bb2121 infusion ]
Percentage of subjects who achieved CR or better according to IMWG Uniform Response Criteria for Multiple Myeloma as assessed by an IRC
2. Overall response rate (ORR) - Cohort 2a, b and c [ Time Frame: Minimum of 2 years after bb2121 infusion ]
Percentage of subjects who achieved partial response (PR) or better according to IMWG Uniform Response Criteria for Multiple Myeloma as assessed by an IRC
3. Time to response (TTR) [ Time Frame: Minimum of 2 years after bb2121 infusion ]
Time from first bb2121 infusion to first documentation of response (PR or greater)
4. Duration of response (DoR) [ Time Frame: Minimum of 2 years after bb2121 infusion ]
Time from first documentation of response (PR or greater) to first documentation of progressive disease (PD) or death from any cause, whichever occurs first
5. Progression-free survival (PFS) [ Time Frame: Minimum of 2 years after bb2121 infusion ]
Time from first bb2121 infusion to first documentation of PD, or death due to any cause, whichever occurs first

6. Time to progression (TTP) [ Time Frame: Minimum of 2 years after bb2121 infusion ]
Time from first bb2121 infusion to first documentation of PD
7. Overall survival (OS) [ Time Frame: Minimum of 2 years after bb2121 infusion ]
Time from first bb2121 infusion to time of death due to any cause
8. Adverse Events (AEs) [ Time Frame: Minimum 5 years after bb2121 infusion ]
Type, frequency, seriousness and severity of adverse events (AEs), adverse events of special interest (AESIs) (including cytokine release syndrome, neurotoxicity and infection), and relationship of AE to study drug.
9. Pharmacokinetics - Cmax [ Time Frame: Minimum 5 years after bb2121 infusion ]
Maximum expansion of bb2121 chimeric antigen receptor (CAR) T cells
10. Pharmacokinetics - tmax [ Time Frame: Minimum 5 years after bb2121 infusion ]
Time to peak of bb2121 CAR T cells
11. Pharmacokinetics - AUC [ Time Frame: Minimum 5 years after bb2121 infusion ]
Area under the curve of CAR T cells
12. Pharmacokinetics - tlast [ Time Frame: Minimum 5 years after bb2121 infusion ]
Time to last measurable CAR T cells
13. Pharmacokinetics - AUC0-28days [ Time Frame: Minimum 5 years after bb2121 infusion ]
Area under the curve of CAR T cells from time zero to Day 28
14. Immunogenicity [ Time Frame: Minimum of 2 years after bb2121 infusion ]
Development of an anti-CAR antibody response
15. Minimal Residual Disease (MRD) negative rate [ Time Frame: Minimum of 2 years after bb2121 infusion ]
Proportion of subjects that are MRD negative
16. Subject-reported outcomes as measured by European Organization for Research and Treatment of Cancer Quality-of-Life questionnaire (EORTC-QLQ-C30) [ Time Frame: Minimum 5 years after bb2121 infusion ]
Questionnaire will be used as a measure of health-related quality of life
17. Subject-reported outcomes as measured by EuroQoL Group EQ-5D-5L Health Questionnaire [ Time Frame: Minimum 5 years after 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
18. Subject-reported outcomes as measured by EORTC-QLQ-MY20 [ Time Frame: Minimum 5 years after bb2121 infusion ]
Is a 20-item myeloma module intended for use among patients varying in disease stage and treatment modality
19. Very good partial response (VGPR) rate - Cohort 2c [ Time Frame: Minimum of 2 years after bb2121 infusion ]
Percentage of subjects who achieved VGPR or better according to IMWG Uniform Response Criteria for Multiple Myeloma as assessed by an IRC

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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:
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. Subject has measurable disease, defined as:
- M-protein (serum protein electrophoresis [sPEP] or urine protein electrophoresis [uPEP]): sPEP ≥ 0.5 g/dL or uPEP ≥ 200 mg/24 hours and/or
- Light chain MM without measurable disease in the serum or urine: Serum immunoglobulin free light chain ≥ 10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio
3. Subjects with one of the following cohort specific requirements:
Cohort 1 RRMM subjects with ≥ 3 prior anti-myeloma treatment regimens:
- Subject must have received at least 3 prior anti-myeloma treatment regimens. Note: induction with or without hematopoietic stem cell transplant and with or without maintenance therapy is considered a single regimen
- Subject must have undergone at least 2 consecutive cycles of treatment for each regimen, unless PD was the best response to the regimen
- Subject must have received prior treatment with a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 antibody
- Subject has evidence of PD on or within 60 days of the most recent prior treatment regimen
- Subject achieved a response (minimal response [MR] or better) to at least 1 prior treatment regimen
Cohort 2 subjects with 1 prior anti-myeloma treatment regimen:
- Subject must have received only 1 prior anti-myeloma treatment regimen. Note: induction with or without hematopoietic stem cell transplant and with or without maintenance therapy is considered a single regimen
- Subject must have the following HR factors:
- R-ISS stage III AND
- Early relapse defined as:
Cohort 2a: PD < 18 months since date of start of initial therapy. Initial therapy must contain induction, ASCT (single or tandem) and lenalidomide containing maintenance. Cohort 2b: PD < 18 months since date of start or initial therapy which must contain at minimum, a proteasome inhibitor, an immunomodulatory agent and dexamethasone Cohort 2c: Subject must have received minimum 3 cycles of induction therapy which must contain at minimum, a proteasome inhibitor, an immunomodulatory agent and dexamethasone. Subjects must have had ASCT (single or tandem AND < VGPR (excluding PD) at first assessment between 70 to 110 days after last ASCT, with initial therapy without consolidation and maintenance. 4. Subject must have Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1 5. Subject must have recovery to Grade 1 or baseline of any non-hematologic toxicities due to prior treatments, excluding alopecia and Grade 2 neuropathy Exclusion Criteria: The presence of any of the following will exclude a subject from enrollment: 1. Subject used any investigational agents within 14 days of leukapheresis 2. Subject received any of the following within the last 14 days of leukapheresis: 1. Plasmapheresis 2. Major surgery (as defined by the investigator) 3. Radiation therapy other than local therapy for myeloma associated bone lesions 4. Use of any systemic anti-myeloma drug therapy 3. Subject with known central nervous system involvement with myeloma 4. Subject has clinical evidence of pulmonary leukostasis and disseminated intravascular coagulation 5. History or presence of clinically relevant central nervous system (CNS) pathology 6. Subject with active or history of plasma cell leukemia, Waldenstrom's macroglobulinemia, POEMS syndrome, or clinically significant amyloidosis 7. Inadequate organ function Subject with a history of Class III or IV congestive heart failure (CHF) or severe nonischemic cardiomyopathy, unstable or poorly controlled angina, myocardial infarction, or ventricular arrhythmia within the previous 6 months prior to starting study treatment 8. Ongoing treatment with chronic immunosuppressants 9. 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 10. Subject has received ASCT within 12 weeks prior to leukapheresis 11. Subject has history of primary immunodeficiency 12. Subject is positive for human immunodeficiency virus (HIV-1), chronic or active hepatitis B or active hepatitis A or C 13. Subject has uncontrolled systemic fungal, bacterial, viral or other infection (including tuberculosis) despite appropriate antibiotics or other treatment 14. Subject with prior history of malignancies, other than MM, unless the subject has been free of the disease for ≥ 5 years 15. Pregnant or lactating women 16. Subject with known hypersensitivity to any component of bb2121 product, cyclophosphamide, fludarabine, and/or tocilizumab

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**CONTACTS AND LOCATIONS**

**Contacts**

Contact:

**Locations**

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| United States, Arizona | Mayo Clinic Arizona | Scottsdale |
| United States, California | UCSF Medical Center | San Francisco |
| United States, Florida | Moffitt Cancer Center | Tampa |
| United States, Georgia | Emory University | Atlanta |
| United States, Massachusetts | Massachusetts General Hospital | Boston |
| United States, Massachusetts | Dana Farber Cancer Institute | Boston |
| United States, Massachusetts | Beth Israel Deaconess Medical Center | Boston |
| United States, Missouri | Washington University | Saint Louis |
| United States, Nebraska | University of Nebraska | Omaha |
| United States, New Jersey | John Theurer Cancer Center at Hackensack University Medical Center | Hackensack |
| United States, New York | Mt Sinai Medical Center - NY | New York |
| United States, New York | Columbia University Medical Center / New York Presbyterian Hospital | New York |
| United States, New York | Memorial Sloan Kettering Cancer Center | New York |
| United States, North Carolina | Levine Cancer Institute | Charlotte |
| United States, Tennessee | Sarah Cannon Research Inst | Nashville |
| United States, Texas | University of Texas Southwestern Medical Center | Dallas |

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| United States, Texas | MD Anderson Cancer Center The University of Texas | Houston |
| United States, Washington | Swedish Cancer Inst | Seattle |
| United States, Wisconsin | Froedtert Hospital BMT Medical College of Wisconsin | Milwaukee |
| France | CHU de Poitiers | Poitiers |
| Germany | Universitaetsklinkum Hamburg-Eppendorf | Hamburg |
| Germany | University Hospital Tuebingen, Department of Internal Medicine | Tuebingen |
| Germany | Universitatsklinikum Würzburg | Würzburg |
| Spain | Clinica Universitaria de Navarra | Pamplona |
| Spain | Hospital Universitario de Salamanca | Salamanca |
| United Kingdom | King's College HospitalGKT School of Medicine | London |

**Sponsors and Collaborators**

Celgene

**Investigator**

Study Director : Lars Sternas, MD, PhD Celgene

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**MORE INFORMATION**

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| **Responsible Party :** | Celgene |
| **ClinicalTrials.gov Identifier :** | NCT03601078 |
| **Other Study ID Numbers :** | BB2121-MM-002, U1111-1216-4209, 2018-000264-28 |
| **First Posted :** | July 26, 2018 |
| **Last Update Posted :** | August 28, 2020 |
| **Last Verified :** | August 2020 |
| **Studies a U.S. FDA-regulated Drug Product:** | Yes |
| **Studies a U.S. FDA-regulated Device Product:** | No |
| **Keywords provided by Celgene:** | *Multiple Myeloma*<br>*bb2121 Relapsed and Refractory Multiple Myeloma*<br>*High Risk Multiple Myeloma* |
| **Additional relevant MeSH terms :** | *Multiple Myeloma* *Neoplasms, Plasma Cell* |