A Dose-finding Study of CC-90009 in Subjects With Relapsed or Refractory Acute Myeloid Leukemia or Relapsed or Refractory Higher-risk Myelodysplastic Syndromes

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT02848001	RECRUITING	JULY 28, 2016	AUGUST 2, 2022

STUDY DESCRIPTION

Brief Summary

CC-90009-AML-001 is a phase 1, open-label, dose escalation and expansion, study in subjects with relapsed or refractory acute myeloid leukemia and relapsed or refractory higher-risk myelodysplastic syndrome.

Condition or Disease: Leukemia, Myeloid, Acute
Myelodysplastic Syndromes

Intervention/treatment: Drug: CC-90009

Phase: Phase 1

DETAILED DESCRIPTION

Study CC-90009-AML-001 is an open-label, Phase 1, dose escalation and expansion, first-in-human clinical study of CC-90009 in subjects with relapsed or refractory acute myeloid leukemia (AML) and relapsed or refractory higher-risk myelodysplastic syndrome.
The dose escalation part (Part A) of the study will evaluate the safety and tolerability of escalating doses of CC-90009 in relapsed and refractory AML. The expansion part, (Part B), will further evaluate the safety and efficacy of CC-90009 administered at or below the maximum tolerated dose (MTD) in selected expansion cohorts of one or more dosing regimens in order to determine the recommended Phase 2 dose (RP2D) for subjects with relapsed or refractory AML and relapsed or refractory higher-risk myelodysplastic syndrome.

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 162 participants

Allocation : Non-Randomized

Intervention Model : Single Group Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Dose-finding Study of CC-90009 in Subjects With Relapsed or Refractory Acute Myeloid Leukemia or Relapsed or Refractory Higher-risk Myelodysplastic Syndromes

Actual Study Start Date: November 2016

Estimated Primary Completion Date: September 2024

Estimated Study Completion Date: September 2025

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: CC-90009 - Part A Will be administered intravenously per dosing schedule in a 28-day cycle.	Drug: CC-90009 CC-90009
Experimental: CC-90009 - Part B - AML and MDS patients Relapsed or refractory AML and MDS subjects. IP will be administered intravenously per dosing schedule determined in Part A	Drug: CC-90009 CC-90009

OUTCOME MEASURES

Primary Outcome Measures:
1. Dose- limiting toxicity (DLT) [Time Frame: Up to 42 days]
Number of participants with a DLT
2. Non-tolerated dose (NTD) [Time Frame: Up to 42 days]
Dose level at which 2 or more of up to 6 evaluable subjects in any dose cohort experience a DLT in Cycle 1 during dose escalation.
3. Maximum tolerated dose (MTD) [Time Frame: Up to 42 days]
Last dose level(s) below the NTD with 0 or 1 out of 6 evaluable subjects experiencing a DLT in Cycle 1 during dose escalation
4. Number of participants with Adverse Events (AEs) [Time Frame: Up to 42 days]
5. Number of participants with laboratory abnormalities [Time Frame: Up to 42 days]
6. Number of participants with vital sign abnormalities [Time Frame: Up to 42 days]
7. Number of participants with electrocardiogram (ECG) abnormalities [Time Frame: Up to 42 days]
8. Number of participants with Eastern Cooperative Oncology Group (ECOG) performance status abnormalities [Time Frame: Up to 42 days]
9. Number of participants with Left Ventricle Ejection Fraction (LVEF) assessment abnormalities [Time Frame: Up to 42 days]
10. Number of participants with physical examination abnormalities [Time Frame: Up to 42 days]

Secondary Outcome Measures:
1. Preliminary efficacy of CC-90009 - acute myeloid leukemia (AML) [Time Frame: Up to 2.5 years]
Determined by response rates of AML by disease response criteria
2. Overall survival [Time Frame: Up to 2.5 years]

3. Relapse-free survival [Time Frame: Up to 2.5 years]
4. Progression-free survival [Time Frame: Up to 2.5 years]
5. Event-free survival [Time Frame: Up to 2.5 years]
6. Duration of remission [Time Frame: Up to 2.5 years]
7. Duration of response [Time Frame: Up to 2.5 years]
8. Time to remission for AML participants [Time Frame: Up to 2.5 years]
9. Time to response for AML participants [Time Frame: Up to 2.5 years]
10. Preliminary efficacy of CC-90009 - Higher-risk myelodysplastic syndromes (HR-MDS) [Time Frame: Up to 2.5 years]
Determined by response rates of HR-MDS by disease response criteria
11. Time to AML transformation [Time Frame: Up to 2.5 years]
12. Time to remission for HR-MDS participants [Time Frame: Up to 2.5 years]
13. Time to response for HR-MDS participants [Time Frame: Up to 2.5 years]
14. Pharmacokinetics-Cmax [Time Frame: Up to Day 11]
Maximum observed concentration in plasma
15. Pharmacokinetics - AUC24 [Time Frame: Up to Day 11]
Area under the plasma concentration time-curve from time 0 to 24 hours
16. Pharmacokinetics - tmax [Time Frame: Up to Day 11]
Time to peak (maximum) plasma concentration
17. Pharmacokinetics - t 1/2 [Time Frame: Up to Day 11]
terminal half-life
18. Pharmacokinetics - CL [Time Frame: Up to Day 11]
Total body clearance of the drug from plasma
19. Pharmacokinetics - Vss [Time Frame: Up to Day 11]
Volume of distribution at steady-state

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:
Men and women ≥ 18 years of age, at the time of signing the ICD (Informed Consent Document). Subject must understand and voluntarily sign an ICD prior to any study-related assessments/procedures being conducted.
Relapsed or refractory AML (Acute Myeloid Leukemia) (Parts A and B) or relapsed or refractory (R/R) higher-risk MDS (Myelodysplastic Syndrome) (HR-MDS) (Part B only) as defined by World Health Organization criteria who are not suitable for other established therapies.
In Part A, R/R AML
In Part B, R/R AML including
Relapsed after allogeneic HSCT or In second or later relapse or Refractory to initial induction or re-induction treatment or Refractory or relapse after HMA treatment (HMA failure defined as primary progression or lack of clinical benefit after a minimum of 6 cycles or unable to tolerate HMA due to toxicity) or Refractory within 1 year of initial treatment (excluding those with favorable risk based on cytogenetics)
In Part B, R/R HR-MDS (Revised International Prognostic Scoring System score (IPSS-R) > 3.5 points, IPSS-R calculated during screening period):
IPSS-R intermediate risk (in combination with more than 10% bone marrow blasts or poor or very poor IPSS-R cytogenetic risk) or IPSS-R high or IPSS-R very high risk Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 to 2. At least 4 weeks (from first dose) has elapsed from donor lymphocyte infusion (DLI) without conditioning.
Subjects must have the following screening laboratory values:
Corrected serum Ca or free (ionized) serum Ca within normal limits (WNL).
o Corrected Ca (mg/dL) = Total Ca (mg/dL) - 0.8 (albumin [g/dL] - 4)
Total White Blood Cell count (WBC) < 25 x 10^9/L prior to first infusion. Prior or concurrent treatment with hydroxyurea to achieve this level is allowed.
Potassium and magnesium within normal limits or correctable with supplements. Aspartate aminotransferase/serum glutamic oxaloacetic transaminase (AST/SGOT) or alanine aminotransferase/serum glutamate pyruvic transaminase (ALT/SGPT) ≤ 2.5 x Upper Limit of Normal (ULN). Uric acid ≤ 7.5 mg/dL (446 µmol/L). Prior and/or concurrent treatment with hypouricemic agents (eg, allopurinol, rasburicase) are allowed. Selected electrolytes within normal limits or correctable with supplements. Serum bilirubin ≤ 1.5 x ULN (upper limit of normal). Estimated serum creatinine clearance of ≥ 60 mL/min using the Cockcroft-Gault equation. Measured creatinine clearance from a 24-hour urine collection is acceptable if clinically indicated. International normalized ratio (INR) < 1.5 x ULN and Partial thromboplastin time (PTT) < 1.5 x ULN. Exclusion Criteria: Subjects with acute promyelocytic leukemia (APL) Subjects with clinical symptoms suggesting active central nervous system (CNS) leukemia or known CNS leukemia. Evaluation of cerebrospinal fluid is only required if there is clinical suspicion of CNS involvement by leukemia during screening. Patients with prior autologous hematopoietic stem cell transplant who, in the investigator's judgment, have not fully recovered from the effects of the last transplant (e.g., transplant related side effects). Prior allogeneic hematopoietic stem cell transplant (HSCT) with either standard or reduced intensity conditioning ≤ 6 months prior to starting CC-90009. Subjects on systemic immunosuppressive therapy post HSCT at the time of screening, or with clinically significant graft-versus-host disease (GVHD). Prior systemic cancer-directed treatments or investigational modalities ≤ 5 half lives or 4 weeks prior to starting CC-90009, whichever is shorter. Hydroxyurea is allowed to control peripheral leukemia blasts. Leukapheresis ≤ 2 weeks prior to starting CC-90009.

CONTACTS AND LOCATIONS

Contacts

Contact: BMS Study Connect Contact Center www.BMSStudyConnect.com 855-907-3286 Clinical.Trials@bms.com
Contact: First line of the email MUST contain NCT # and Site #.

Locations

United States, Connecticut	Yale Cancer Center	New Haven
United States, Connecticut	Yale Cancer Center	New Haven
United States, Illinois	Northwestern Memorial	Chicago
United States, Massachusetts	Dana Farber Cancer Institute	Boston

United States, Missouri	Washington University Siteman Cancer Center	Saint Louis
United States, Missouri	Washington University Siteman Cancer Center	Saint Louis
United States, New Jersey	Hackensack University Medical Center	Hackensack
Canada, Ontario	Princess Margaret Hospital University Health Network	Toronto
France	Institut Paoli Calmettes	Marseille Cedex 9
France	Hopital Lyon Sud	Pierre Benite
France	Institut Claudius Regaud, IUCT-Oncopole	Toulouse
Norway	Haukeland University Hospital	Bergen
Norway	Oslo University Hospital, Rikshospitalet HF	Oslo
Spain	Hospital Germans Trias I Pujol	Badalona
Spain	Local Institution - 603	Badalona
Spain	H Clinic I Provincial	Barcelona
Spain	Local Institution - 602	Barcelona
Spain	MD Anderson Cancer Center - Madrid	Madrid
Spain	Clinica Universidad de Navarra	Pamplona
Spain	Hospital Clinico Universitario de Salamanca	Salamanca
Spain	Hosptial La Fe	Valencia
United Kingdom	Clatterbridge Cancer Centre - Liverpool	Liverpool
United Kingdom	Local Institution - 301	Oxford
United Kingdom	The Churchill Hospital	Oxford

Sponsors and Collaborators

Celgene

Investigator

Study Director :	Bristol-Myers Squibb	Bristol-Myers Squibb

MORE INFORMATION

Other Publications

Surka C, Jin L, Mbong N, Lu CC, Jang IS, Rychak E, Mendy D, Clayton T, Tindall E, Hsu C, Fontanillo C, Tran E, Contreras A, Ng SWK, Matyskiela M, Wang K, Chamberlain P, Cathers B, Carmichael J, Hansen J, Wang JCY, Minden MD, Fan J, Pierce DW, Pourdehnad M, Rolfe M, Lopez-Girona A, Dick JE, Lu G. CC-90009, a novel cereblon E3 ligase modulator, targets acute myeloid leukemia blasts and leukemia stem cells. Blood. 2021 Feb 4;137(5):661-677. doi: 10.1182/blood.2020008676.

Responsible Party : Celgene

ClinicalTrials.gov Identifier : NCT02848001

Other Study ID Numbers : CC-90009-AML-001, 2017-001535-39

First Posted : July 28, 2016

Last Update Posted : August 2, 2022

Last Verified : August 2022

Keywords provided by Celgene:

CC-90009
Hematologic Cancers
Leukemia
Acute Myeloid Leukemia Myelodysplastic Syndrome
AML
MDS

Additional relevant MeSH terms :

Leukemia	*Pathologic Processes*
Leukemia, Myeloid	*Neoplasms by Histologic Type*
Leukemia, Myeloid, Acute	*Neoplasms*
Preleukemia	*Bone Marrow Diseases*
Myelodysplastic Syndromes	*Hematologic Diseases*
Syndrome	*Precancerous Conditions*
Disease	