A Safety and Efficacy Study of CC-90009 Combinations in Subjects With Acute Myeloid Leukemia

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT04336982	RECRUITING	APRIL 7, 2020	JULY 8, 2022

STUDY DESCRIPTION

Brief Summary

CC-90009-AML-002 is an exploratory Phase 1b, open-label, multi-arm trial to evaluate the safety and efficacy of CC-90009 in combination with anti-leukemia agents in participants with acute myeloid leukemia (AML).

Condition or Disease: Leukemia, Myeloid, Acute

Intervention/treatment: Drug: CC-90009
Drug: Venetoclax
Drug: Azacitidine
Drug: Gilteritinib

Phase: Phase 1/Phase 2

DETAILED DESCRIPTION

Study CC-90009-AML-002 is an open-label, multi-arm, parallel multi-cohort, multicenter, Phase 1b study to determine the safety, tolerability, PK, and efficacy of CC 90009 in combination with anti-leukemia agents used for the treatment of AML. CC 90009 will be given as a combination therapy to subjects with newly diagnosed (ND) or relapsed or refractory (R/R) AML.
The dose and schedule finding part (Part A) of the study will evaluate the safety, PK and PD data, and preliminary efficacy information and determine the Part B dose and schedule for each arm.
The expansion part (Part B) of the study will further evaluate the safety and efficacy of the CC-90009 containing combination at or below the maximum tolerated dose (MTD) in the selected cohorts in order to determine the recommended Phase 2 dose (RP2D) for subjects with AML.

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 43 participants

Allocation : Non-Randomized

Intervention Model : Parallel Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Safety and Efficacy Study of CC-90009 Combinations in Subjects With Acute Myeloid Leukemia

Actual Study Start Date: August 2020

Estimated Primary Completion Date: January 2025

Estimated Study Completion Date: January 2025

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: CC-90009 in combination with venetoclax and azacitidine CC-90009 will be administered intravenously per dosing schedule in a 28-day cycle. Venetoclax will be administered orally QD. Azacitidine will be administered intravenously or subcutaneously on planned dosing days for each cycle.	Drug: CC-90009 Injection Drug: Venetoclax Tablet Drug: Azacitidine Injection
Experimental: CC-90009 in combination with gilteritinib CC-90009 will be administered intravenously per dosing schedule in a 28-day cycle. Gilteritinib will be administered orally QD.	Drug: Gilteritinib Tablet

OUTCOME MEASURES

Primary Outcome Measures: 1. Dose Limiting Toxicity (DLT) [Time Frame: Up to 28 days]
Number of participants with a DLT
2. Adverse Events (AEs) [Time Frame: Up to 28 days after last dose of study drug.]
An AE is any noxious, unintended, or untoward medical occurrence that may appear or worsen in a subject during the course of a study. It may be a new intercurrent illness, a worsening concomitant illness, an injury, or any concomitant impairment of the subject's health, including laboratory test values, regardless of etiology.

Secondary Outcome Measures: 1. Complete Remission Rate (CRR), [Time Frame: Up to 3 years]
is defined as the rate for any type of CR or CRh
2. Objective Response Rate (ORR) [Time Frame: Up to 3 years]
includes all responses of complete remissions (CRs), Morphologic leukemia-free state (MLFS), and Partial remission (PR)

3. Progression Free Survival (PFS) [Time Frame: Up to 3 years]
is defined as the time from the first dose of study drug(s) to the first occurrence of relapse or progression or death from any cause
4. Overall Survival (OS) [Time Frame: Up to 3 years]
is measured as the time from the first dose of study drug(s) to death due to any cause and will be analyzed in a manner similar to that described for PFS.
5. Duration of Remission [Time Frame: Up to 3 years]
is measured from the time when criteria for CR/CRh/PR are first met (whichever is first recorded) until the first date at which relapse, or progressive disease is objectively documented.
6. Time to Remission [Time Frame: Up to 3 years]
is measured from the time when criteria for CR/CRh/PR are first met (whichever is first recorded)
7. Pharmacokinetics - Cmax [Time Frame: Until last CC-90009 dose in Cycle 3 (each cycle is 28 days. CC-90009 dosing days are Days 1-5 in Cycle 3)]
observed maximum concentration in plasma
8. Pharmacokinetics - AUC24 [Time Frame: Until last CC-90009 dose in Cycle 3 (each cycle is 28 days. CC-90009 dosing days are Days 1-5 in Cycle 3)]
area under the plasma concentration time-curve from time 0 to 24 hours postdose
9. Pharmacokinetics - t1/2 [Time Frame: Until last CC-90009 dose in Cycle 3 (each cycle is 28 days. CC-90009 dosing days are Days 1-5 in Cycle 3)]
terminal half life

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:
Adult subject must understand and voluntarily sign an ICF prior to any study-related assessments/procedures being conducted.
Arm A (CC-90009 + venetoclax/azacitidine):
Part A: Newly diagnosed AML with poor/adverse risk genetic abnormalities and is ≥ 75 years of age or intensive chemotherapy ineligible OR Part A: Refractory AML and is ≥ 18 years of age Part B: Newly diagnosed AML and is ≥ 75 years of age or intensive chemotherapy ineligible
Arm B (CC-90009 + gilteritinib):
Subject is ≥ 18 years of age. Fms-like tyrosine kinase 3 (FLT3) mutation positive. Gilteritinib treatment naïve Subject has Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2.
Subject must have the following screening laboratory values:
Total White Blood Cell count (WBC) < 25 x 10^9/L prior to study treatments. Treatment with hydroxyurea to achieve this level is allowed. Selected electrolytes within normal limits or correctable with supplements. Participant must have adequate liver function as demonstrated by: Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 2.5 x upper limit of normal (ULN) and bilirubin ≤ 1.5 x ULN Participant has adequate renal function as demonstrated by an estimated serum creatinine clearance of ≥ 60 mL/min using the Cockcroft-Gault equation. Agree to follow the CC-90009 Pregnancy Prevention Plan (PPP) and combination agents' requirements. Exclusion Criteria: Subject with acute promyelocytic leukemia (APL) Subject has received systemic anticancer therapy (including investigational therapy) or radiotherapy < 28 days or 5 half-lives, whichever is shorter, prior to the start of study treatment Patients with prior autologous hematopoietic stem cell transplant (HSCT) who, in the investigator's judgment, have not fully recovered from the effects of the last transplant (eg, transplant related side effects) Prior allogeneic HSCT with either standard or reduced intensity conditioning ≤ 6 months prior to dosing Subject on systemic immunosuppressive therapy post HSCT at the time of screening, or with clinically significant graft-versus-host disease (GVHD). The use of topical steroids for ongoing skin or ocular GVHD is permitted Subject has persistent, clinically significant non-hematologic toxicities from prior therapies which have not recovered to < Grade 2 Subject has or is suspected of having central nervous system (CNS) leukemia. Evaluation of cerebrospinal fluid is only required if CNS involvement by leukemia is suspected during screening. Disorders or conditions disrupting normal calcium homeostasis or preventing calcium supplementation. Impaired cardiac function or clinically significant cardiac diseases, including any of the following: Left ventricular ejection fraction (LVEF) 450 ms (Arm B) on Screening electrocardiogram (ECG) Unstable angina pectoris or myocardial infarction ≤ 6 months prior to starting study treatments or unstable arrhythmia. Cardiovascular disability status of New York Heart Association Class ≥2. Class 2 is defined as cardiac disease in which patients are comfortable at rest but ordinary physical activity results in fatigue, palpitations, dyspnea, or anginal pain. Subject is a pregnant or lactating female
Additional exclusion criteria based on combination agent:
a. For Combination Arm A (venetoclax/azacitidine):
Received strong or moderate CYP3A inhibitors or inducers or P-gp inhibitors within 7 days prior to initiation of first venetoclax dose. Subject has consumed grapefruit, grapefruit products, Seville oranges (including marmalade containing Seville oranges), or Star fruit within 3 days prior to first venetoclax dose through last dose of venetoclax.
Previous SARS-CoV-2 infection within 10 days for mild or asymptomatic infections or 20 days for severe/critical illness prior to C1D1.
a. Acute symptoms must have resolved and based on investigator assessment in consultation with the medical monitor, there are no sequelae that would place the participant at a higher risk of receiving study treatment.
Previous SARS-CoV-2 vaccine within 14 days of C1D1.

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 the NCT# and Site #

Locations

United States, California	University of California, San Francisco	San Francisco
United States, California	University Of California, San Francisco	San Francisco
United States, Connecticut	Yale New Haven Hospital	New Haven
United States, Massachusetts	Dana-Farber/Mass General Brigham Cancer Care, Inc	Boston

United States, Missouri	Washington University School of Medicine	Saint Louis
United States, Missouri	Washington University School Of Medicine	Saint Louis
United States, New Jersey	Hackensack University Medical Center	Hackensack
United States, Texas	The University of Texas - MD Anderson Cancer Center	Houston
United States, Texas	The University of Texas - MD Anderson Cancer Center	Houston
United States, Washington	Fred Hutchinson Cancer Research Center	Seattle
Canada, Alberta	University of Alberta	Edmonton
Canada, Ontario	Princess Margaret Cancer Centre	Toronto
Canada, Quebec	Hopital Maisonneuve-Rosemont	Montreal
France	Institut Paoli-Calmettes	Marseille
France	Local Institution - 402	Marseille
France	Hopital Haut Leveque	Pessac Cedex
France	Local Institution - 401	Pessac Cedex
France	Institut Universitaire du Cancer de Toulouse (IUCT) - Oncopole	Toulouse Cedex 9
France	Local Institution - 404	Toulouse Cedex 9
United Kingdom	John Radcliffe Hospital	Oxford
United Kingdom	Local Institution - 301	Oxford

Sponsors and Collaborators

Celgene

AbbVie

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 :	NCT04336982
Other Study ID Numbers :	CC-90009-AML-002, U1111-1247-5619, 2019-001681-15
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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:	*CC-90009* *Venetoclax* *Azacitidine* *Gilteritinib Hematologic cancers* *Leukemia* *Acute myeloid leukemia* *AML*	
Additional relevant MeSH terms :	*Leukemia* *Leukemia, Myeloid* *Leukemia, Myeloid, Acute*	*Neoplasms by Histologic Type* *Neoplasms*