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	JANUARY 13, 2021

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 subjects 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 : 66 participants

Intervention Model : Parallel Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: An Exploratory Phase 1/2 Open-Label Multi-Arm Trial to Evaluate the Safety and Efficacy of CC-90009 Combinations in Subjects With Acute Myeloid Leukemia

Actual Study Start Date: August 2020

Estimated Primary Completion Date: April 2023

Estimated Study Completion Date: April 2023

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. Maximum Tolerated Dose (MTD) [Time Frame: Up to 28 days.]
The highest dose with DLT rate in Cycle 1 being lower than or close to the target level 0.3 and the toxicity probability within (0.25, 0.35) interval.

	3. 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] is defined as the rate for all types of CRs and PR for AML. 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

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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:
1. Adult subject must understand and voluntarily sign an ICF prior to any study-related assessments/procedures being conducted.
2. Arm A (CC-90009 + venetoclax/azacitidine):
1. Newly diagnosed AML and is ≥ 75 years of age or intensive chemotherapy ineligible OR
2. Refractory AML and is ≥ 18 years of age
3. Arm B (CC-90009 + gilteritinib):
1. Subject is ≥ 18 years of age.
2. FLT3-ITD positive relapsed or refractory AML.
3. Gilteritinib treatment naïve
4. Subject has Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2.
5. Subject must have the following screening laboratory values:
- Total White Blood Cell count (WBC) < 25 x 10^9 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. 6. Agree to follow the CC-90009 Pregnancy Prevention Plan (PPP) and combination agents' requirements. Exclusion Criteria: 1. Subject with acute promyelocytic leukemia (APL) 2. 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 3. 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) 4. Prior allogeneic HSCT with either standard or reduced intensity conditioning ≤ 6 months prior to dosing 5. 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 6. Subject has persistent, clinically significant non-hematologic toxicities from prior therapies which have not recovered to < Grade 2 7. 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 8. Impaired cardiac function or clinically significant cardiac diseases, including any of the following: 1. Left ventricular ejection fraction (LVEF) 450 ms (Arm B) on Screening electrocardiogram (ECG)
6. Unstable angina pectoris or myocardial infarction ≤ 6 months prior to starting study treatments or unstable arrhythmia.
7. 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.
suspected during screening.
9. Subject is a pregnant or lactating female
10. Additional exclusion criteria based on combination agent:
1. 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.

CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

United States, California	University of California, San Francisco	San Francisco

United States, Connecticut	Yale New Haven Hospital	New Haven
United States, Massachusetts	Dana-Farber Cancer Institute	Boston
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, 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	Hopital Haut Leveque	Pessac Cedex
France	Institut Universitaire du Cancer de Toulouse (IUCT) - Oncopole	Toulouse Cedex 9
United Kingdom	John Radcliffe Hospital	Oxford

Sponsors and Collaborators

Celgene

AbbVie

Investigator

Study Director : Michael Pourdehnad, M.D. Celgene

MORE INFORMATION

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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Last Update Posted :	January 13, 2021
Last Verified :	January 2021
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:	*Acute myeloid leukemia* *Leukemia* *CC-90009* *Venetoclax Azacitidine* *Gilteritinib* *Hematologic cancers* *AML*
Additional relevant MeSH terms :	*Leukemia* *Leukemia, Myeloid* *Leukemia, Myeloid, Acute*