A Safety and Preliminary Efficacy Study of CC-99282 in Combination With Obinutuzumab in Subjects With Relapsed or Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT04434196	RECRUITING	JUNE 16, 2020	AUGUST 28, 2020

STUDY DESCRIPTION

Brief Summary

CC-99282-CLL-001 study is a Phase IB dose escalation and expansion clinical study of CC-99282 administered in combination with Obinutuzumab in subjects with relapsed or refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma.

Condition or Disease: Lymphoma, Non-Hodgkin

Intervention/treatment: Drug: CC-99282
Drug: Obinutuzumab

Phase: Phase 1

DETAILED DESCRIPTION

All eligible subjects must be relapsed or refractory to at least 2 prior lines of therapy, one of which must have included an inhibitor of B-cell receptor signaling (approved Bruton's tyrosine kinase inhibitor [BTKi] or Phosphoinositide 3-kinase inhibitor [PI3Ki]) or venetoclax. The dose escalation (Part A) will evaluate the safety, tolerability, and PK of escalating doses of CC-99282 given in combination with intravenous obinutuzumab to determine the MTD and RP2D of CC-99282 when given in combination with obinutuzumab.The dose expansion (Part B) may occur at the MTD established in the dose escalation phase, or at an alternative tolerable dosing schedule, based on review of safety, PK and PD data from Part A.

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 50 participants

Intervention Model : Sequential Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Phase 1B, Multicenter, Open-label Study to Determine the Safety, Pharmacokinetics and Preliminary Efficacy of CC-99282 in Combination With Obinutuzumab in Subjects With Relapsed or Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Estimated Study Start Date: August 2020

Estimated Primary Completion Date: June 2024

Estimated Study Completion Date: May 2025

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: CC-99282 + obinutuzumab Escalating doses of CC-99282 administered orally once daily on intermittent schedules with obinutuzumab IV infusion 1000 mg up to 2 years in Part A. CC-99282 administered orally once daily at MTD or alternative tolerating dosing schedule with obinutuzumab IV infusion 1000 mg up to 2 years in Part B.	Drug: CC-99282 CC-99282 Drug: Obinutuzumab Obinutuzumab

OUTCOME MEASURES

Primary Outcome Measures:
1. Dose Limiting Toxicity (DLT) [Time Frame: Up to Cycle 2 Day 14 (each cycle is 28 days)]
Number of subjects with a DLT
2. Maximum tolerated dose (MTD) [Time Frame: Up to Cycle 2 Day 14 (each cycle is 28 days]
The highest dose of CC-99282 in combination with obinutuzumab associated with acceptable safety and tolerability
3. Adverse Events (AEs) [Time Frame: From first subjects first visit until 28 days after last subject discontinued study treatment]
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. Any worsening (ie, any clinically significant adverse change in the frequency or intensity of a preexisting condition) should be considered an AE.

Secondary Outcome Measures:
1. Pharmacokinetics - Cmax [Time Frame: Up to Cycle 2 Day 14 (each cycle is 28 days)]
Maximum observed plasma concentration
2. Pharmacokinetics - AUC [Time Frame: Up to Cycle 2 Day 14 (each cycle is 28 days)]
Area under the plasma concentration-time curve
3. Pharmacokinetics - Tmax [Time Frame: Up to Cycle 2 Day 14 (each cycle is 28 days)]
Time to Cmax

4. Pharmacokinetics - t1/2 [Time Frame: Up to Cycle 2 Day 14 (each cycle is 28 days)]
Terminal-phase elimination half-life
5. Pharmacokinetics - CL/F [Time Frame: Up to Cycle 2 Day 14 (each cycle is 28 days)]
Apparent total clearance of the drug from plasma after oral administration
6. Pharmacokinetics - V/F [Time Frame: Up to Cycle 2 Day 14 (each cycle is 28 days)]
Apparent volume of distribution during terminal phase after non-intravenous administration
7. Objective response rate (ORR) [Time Frame: Up to approximately 3 years]
Sum of complete response (CR), complete response with incomplete marrow recovery (CRi), nodular partial response (nPR), partial response (PR), partial response with lymphocytosis (PRL) determined by iwCLL criteria
8. Duration of response (DoR) [Time Frame: Up to approximately 3 years]
Time from first documentation of response (≥ PR) to the first documentation of PD or death
9. Progression free survival [Time Frame: Up to approximately 3 years]
Time from first dose of CC-99282 to the first occurrence of disease progression or death from any cause
10. Overall survival [Time Frame: Up to approximately 3 years]
Time from first dose of CC-99282 to death from any cause
11. Complete response with incomplete marrow recovery (CRi) [Time Frame: Up to approximately 3 years]
As assessed by International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria
12. Nodular partial response (nPR) [Time Frame: Up to approximately 3 years]
As assessed by iwCL and International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria
13. Partial response (PR) [Time Frame: Up to approximately 3 years]
As assessed by iwC and International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria
14. Partial response with lymphocytosis (PRL) [Time Frame: Up to approximately 3 years]
As assessed by iwCLL and International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria

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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. Subject is ≥18 years of age
2. Eastern Cooperative Oncology Group (ECOG) performance status of 0-2.
3. Must have a documented diagnosis of CLL/SLL requiring treatment (IwCLL Guidelines for the Diagnosis and Treatment of CLL). In addition presence of clinically measurable disease determined by at least one of the factors listed:
- nodal lesion that measures ≥ 1.5 cm in longest dimension (LD) and ≥ 1.0 cm in longest perpendicular dimension (LPD), or
- spleen that measures ≥ 14 cm in longest vertical dimension (LVD) with a minimum of 2 cm enlargement, or
- liver that measures ≥ 20 cm in LVD with a minimum of 2 cm enlargement, or
- peripheral blood B lymphocyte count > 5000/uL
4. All eligible subjects must be relapsed after or be refractory to >2 prior lines of therapy one of which must have included an approved BTK inhibitor.
5. Must meet the following laboratory parameters:
1. Absolute neutrophil count (ANC) ≥ 1,500 cells/mm3 or ≥ 1000 cells/mm3 if secondary to bone marrow involvement by disease.
2. Platelet count ≥ 100,000 cells/mm3 (100 x 109/L) or ≥ 50,000 cells/mm3 (50 x 109/L) if secondary to bone marrow involvement by disease.
3. Serum aspartate transaminase (AST/SGOT) or alanine transaminase (ALT/SGPT) < 3.0 x upper limit of normal (ULN). 4. Serum bilirubin < 1.5 x ULN unless due to Gilbert's syndrome. 5. Calculated creatinine clearance of ≥ 60 ml/min. Exclusion Criteria: 1. Presence of any significant medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from participating in the study. 2. Prior allogeneic stem cell transplant (SCT)/bone marrow transplant within 12 months of signing the ICD. Subjects who received allogeneic SCT ≥ 12 months before signing the ICD may be eligible provided there is no ongoing graft-versus-host disease and no ongoing immune suppression therapy. 3. Subject has received prior CAR-T or other T-cell targeting treatment (approved or investigational) ≤ 4 weeks prior to starting CC-99282. 4. Subject has received prior therapy with CRBN-modulating drug (eg, lenalidomide, avadomide/CC-122, pomalidomide) ≤ 4 weeks prior to starting CC-99282. 5. History of second malignancies with life expectancy of ≤ 2 years or requirement of therapy that would confound study results. 6. Peripheral neuropathy ≥ Grade 2. 7. History of hypersensitivity to lenalidomide, pomalidomide, thalidomide. 8. Impaired cardiac function or clinically significant cardiac disease. 9. Persistent diarrhea or malabsorption ≥ NCI CTCAE Grade 2, despite medical management. 10. Active disease transformation (ie, Richter's Syndrome) 11. Uncontrolled/active autoimmune hemolytic anemia or thrombocytopenia

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CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

United States, Massachusetts	Dana Farber Cancer Institute	Boston
United States, New York	Memorial Sloan-Kettering Cancer Center	New York
United States, Ohio	The Ohio State University Comprehensive Cancer Center	Columbus
United States, Oregon	Oregon Health and Science University	Portland
United States, Texas	Southwestern Medical Center- Harold C Simmons Comprehensive Cancer Center	Dallas
Austria	Universitaetsklinik fuer Innere Medizin V	Innsbruck
Austria	Landeskrankenhaus Salzburg	Salzburg
Austria	Allgemeinen Krankenhaus (AKH) Wien - Medizinische Universitaet Wien	Wien
Canada, Ontario	Princess Margaret Hospital University Health Network	Toronto

Canada, Quebec	Sir Mortimer B. Davis - Jewish Genl	Montreal
Spain	Hospital Universitario Vall D hebron	Barcelona
Spain	Hospital 12 de Octubre	Madrid
Spain	Clinica Universidad de Navarra	Pamplona
Spain	Universitario de Salamanca - Hospital Clinico	Salamanca
Spain	Hospital Clinico Universitario de Valencia	Valencia

Sponsors and Collaborators

Celgene

Investigator

Study Director :	Poliana Patah, MD, PhD	Bristol-Myers Squibb

MORE INFORMATION

Responsible Party :	Celgene
ClinicalTrials.gov Identifier :	NCT04434196
Other Study ID Numbers :	CC-99282-CLL-001, U1111-1251-4261, 2019-003228-18
First Posted :	June 16, 2020
Last Update Posted :	August 28, 2020
Last Verified :	August 2020
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:	*Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma* *Efficacy* *CC-99282* *Obinutuzumab Relapsed* *Refractory* *Safety*
Additional relevant MeSH terms :	*Leukemia, Lymphocytic, Chronic, B-Cell* *Lymphoma, Non-Hodgkin* *Leukemia, Lymphoid* *Lymphoma* *Leukemia*