A Safety and Preliminary Efficacy Study of CC-99282, Alone and in Combination With Rituximab in Subjects With Relapsed or Refractory Non-hodgkin Lymphomas (R/R NHL)

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT03930953	RECRUITING	APRIL 29, 2019	JANUARY 14, 2021

STUDY DESCRIPTION

Brief Summary

CC-99282-NHL-001 study is a Phase I dose escalation and expansion clinical study of CC-99282 administered alone and in combination with rituximab in subjects with relapsed or refractory non-hodgkin Lymphomas (R/R NHL).

Condition or Disease: Lymphoma, Non-Hodgkin

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

Phase: Phase 1

DETAILED DESCRIPTION

Subjects with R/R NHL who have failed at least 2 lines of therapy (or have received at least one prior line of standard therapy and are not eligible for any other therapy).
The dose escalation will evaluate the safety and tolerability of escalating doses of CC-99282 in R/R DLBCL and/or R/R FL subjects to determine the MTD of CC-99282 as monotherapy.
The dose expansion will further evaluate the safety and preliminary efficacy of single agent CC-99282 administered at or below MTD in subjects with R/R DLBCL and NHL. Part B will also evaluate the safety and preliminary efficacy of CC-99282 in combination with rituximab in subjects with R/R DLBCL and R/R FL.

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 100 participants

Intervention Model : Sequential Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Phase 1, Multi-center, Open-label, Study to Assess the Safety, Pharmacokinetics, and Preliminary Efficacy of an Orally Available Small Molecule CC-99282 Alone and in Combination With Rituximab in Subjects With Relapsed or Refractory Non-Hodgkin Lymphoma (R/R iNHL).

Actual Study Start Date: May 2019

Estimated Primary Completion Date: June 2023

Estimated Study Completion Date: May 2024

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: Administration of CC-99282 Escalating doses of CC-99282 administered orally once daily on intermittent schedules up to 2 years.	Drug: CC-99282 CC-99282
Experimental: CC-99282 + rituximab CC-99282 administered orally once daily on intermittent schedule with rituximab intravenously (IV) 375 mg/m2 weekly in Cycle 1, every 28 days in C2-6, then every 8 weeks through 2 years.	Drug: CC-99282 CC-99282 Drug: rituximab rituximab

OUTCOME MEASURES

Primary Outcome Measures:
1. Dose Limiting Toxicity (DLT) [Time Frame: up to 28 days in Cycle 1]
Number of subjects with a DLT
2. Maximum tolerated dose (MTD) [Time Frame: up to 28 days in cycle 1]
The highest dose of CC-99282 associated with acceptable safety and tolerability
3. Adverse Events (AEs) [Time Frame: From the time of consent at screening until 28 days after the subject discontinued study treatment (up to 2 years)]
Type, frequency, seriousness, severity and relationship of AEs to CC-99282 and rituximab; changes from baseline in clinically-relevant physical findings, vital signs, selected analytes, ECGs, LVEF and ECOG

Secondary Outcome Measures:
1. Pharmacokinetics - Cmax [Time Frame: Cycle 1 to Cycle 4 Day 15 (each cycle is 28 days)]
Maximum observed plasma concentration
2. Pharmacokinetics - AUC [Time Frame: Cycle 1 to Cycle 4 Day 15 (each cycle is 28 days)]
Area under the plasma concentration-time curve

3. Pharmacokinetics - Tmax [Time Frame: Cycle 1 to Cycle 4 Day 15 (each cycle is 28 days)]
Time to Cmax
4. Pharmacokinetics - t1/2 [Time Frame: Cycle 1 to Cycle 4 Day 15 (each cycle is 28 days)]
Terminal-phase elimination half-life
5. Pharmacokinetics - CL/F [Time Frame: Cycle 1 to Cycle 4 Day 15 (each cycle is 28 days)]
Apparent total clearance of the drug from plasma after oral administration
6. Pharmacokinetics - V/F [Time Frame: Cycle 1 to Cycle 4 Day 15 (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 partial response (PR) plus complete response (CR) determined by the Lugano Classification for NHL and by the modified International PCNSL collaborative Group (IPCG) criteria
8. Time to response (TTR) [Time Frame: up to approximately 3 years]
Time from first dose of CC-99282 to the first documentation of response ≥ PR
9. 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
10. 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
11. Overall survival [Time Frame: up to approximately 3 years]
Time from first dose of CC-99282 to death from any cause

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 at the time of signing the informed consent form (ICF).
2. Subject has a history of NHL with relapsed or refractory disease
3. Subject has an Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2.
4. Subjects must have the following laboratory values:
1. Absolute neutrophil count (ANC) ≥ 1.5 x 109/L without growth factor support for 7 days (14 days if pegfilgastrim)
2. Hemoglobin (Hgb) ≥ 8 g/dL
3. Platelets (plt) ≥ 75 x 109/L without transfusion for 7 days
4. Serum bilirubin ≤ 1.5 x ULN (upper limit of normal).
5. AST/SGOT and ALT/SGPT ≤ 2.5X ULN
6. Estimated serum creatinine clearance of ≥ 60 mL/min using the Cockcroft-Gault equation.
5. Agree to follow the CC-99282 Pregnancy Prevention Plan (PPP)
Exclusion Criteria:
The presence of any of the following will exclude a subject from enrollment:
1. Subject has life expectancy ≤ 2 months.
2. Subject has received prior systemic anti-cancer treatment (approved or investigational) ≤ 5 half-lives or 4 weeks prior to starting CC-99282, whichever is shorter.
3. Subject has symptomatic CNS involvement of disease (does not apply to PCNSL subjects in Part B).
4. Persistent diarrhea or malabsorption≥ Grade 2 , despite medical management
5. Subject is on chronic systemic immunosuppressive therapy or corticosteroids (eg, prednisone or equivalent not to exceed 10 mg per day within the last 14 days) or subjects with clinically significant graft-versus-host disease (GVHD).
6. Subject had prior autologous SCT ≤ 3 months prior to starting CC 99282. If subject had prior autologous SCT > 3 months prior to the start of CC-99282, any treatment-related toxicity is unresolved (grade > 1).
7. Subject had prior allogeneic SCT with either standard or reduced intensity conditioning ≤ 6 months prior to starting CC-99282. If subject had prior allogenic SCT > 6 months prior to the start of CC-99282, any treatment-related toxicity is unresolved (grade > 1).
8. Impaired cardiac function or clinically significant cardiac disease

---

CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

United States, Florida	H Lee Moffitt Cancer Center	Tampa
United States, Missouri	Washington University	Saint Louis
United States, New Jersey	Hackensack University Medical Center	Hackensack
United States, Texas	MD Anderson Cancer Center	Houston
Canada, Alberta	Cross Cancer Institute University of Alberta	Edmonton
Canada, Ontario	Princess Margaret Cancer Centre	Toronto
Canada, Quebec	Jewish General Hospital	Montreal
France	Centre Hospitalier Lyon-Sud	Pierre-Benite CEDEX
France	Gustave Roussy	Villejuif CEDEX
Italy	Azienda Ospedaliera Papa Giovanni XXIII	Bergamo

Italy	Istituto Nazionale per lo Studio e la Cura dei Tumori "Fondazione Giovanni Pascale"	Napoli
Spain	Vall d´Hebron University Hospital	Barcelona
Spain	Fundacion Jimenez Daaz	Madrid
Spain	Hospital La Paz	Madrid
Spain	Hospital Universitario Virgen De La Victoria	Malaga

Sponsors and Collaborators

Celgene

Investigator

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

MORE INFORMATION

Responsible Party :	Celgene
ClinicalTrials.gov Identifier :	NCT03930953
Other Study ID Numbers :	CC-99282-NHL-001, U1111-1224-5399, 2018-003235-29
First Posted :	April 29, 2019
Last Update Posted :	January 14, 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:	*Non-Hodgkin Lymphomas* *Safety* *Rituximab* *Relapsed Refractory* *CC-99282* *Efficacy*
Additional relevant MeSH terms :	*Lymphoma* *Lymphoma, Non-Hodgkin*