A Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Efficacy of CC-90010 in Subjects With Advanced Solid Tumors and Relapsed/Refractory Non-Hodgkin's Lymphomas

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT03220347	RECRUITING	JULY 18, 2017	AUGUST 5, 2020

STUDY DESCRIPTION

Brief Summary

Study CC-90010-ST-001 is an open-label, Phase 1a, dose escalation and expansion, First-in-human (FIH) clinical study of CC-90010 in subjects with advanced or unresectable solid tumors and relapsed and/or refractory advanced Non-Hodgkin's lymphoma (NHL). The dose escalation part (Part A) of the study will explore escalating oral doses of CC-90010 to estimate the maximum tolerated dose (MTD) of CC-90010. The expansion part (Part B) will further evaluate the safety and efficacy of CC-90010 administered at or below the MTD in the following cohorts: Cohort 1: relapsed and/or refractory DLBCL approximately 20-25 evaluable subjects at 45 mg CC-90010 4-days-on/24-days-off in each 28-day cycle Cohort 2: advanced BCC -enrollment stopped due to recruitment challenges Cohort 3: relapsed and/or refractory DLBCL -approximately 15 evaluable subjects at 30mg CC-90010 3-dayson/11-days-offin each 28-day cycle The food effect assessment (Part C, Spain only) will evaluate the impact of food on CC-90010 when administered at the RP2D of 45 mg 4-days-on/24-days-off (180 mg per 28-day cycle), by comparison of the PK parameters following fasted and fed (high-fat, high-calorie meal) conditions.

Condition or Disease: Lymphoma, Non-Hodgkin
Neoplasms

Intervention/treatment: Drug: CC-90010

Phase: Phase 1

DETAILED DESCRIPTION

Parts A, B and C will consist of 3 periods: Screening, Treatment and Follow-up.
Screening Period:
The Screening Period starts 28 days (± 3 days) prior to first dose of CC-90010. The informed document (ICD) must be signed and dated by the subject and the administering staff prior to the start of any other study procedures. All screening tests and procedures must be completed within the 28 days (±3 days) prior to the first dose of CC-90010.
Treatment Period:
During the Treatment Period, CC-90010 was initially administered orally once daily for 3 consecutive days followed by 4 consecutive days off drug every week (3/7-days schedule) in each 28-day cycle in Part A. Alternative dosing schedules (eg, 2-days-on/5-days- off each week, 3-days-on/4-days-off every other week, 4-days on/24 days off) may be evaluated one dosing schedule at a time or ≥ 2 dosing schedules given in parallel, based on the review of available safety, PK, pharmacodynamic (PD), and efficacy data by the SRC.
Following completion of dose escalation in Part A, selected expansion cohorts will receive CC-90010 in Part B. The SRC determined the RP2D for Part B to be 45 mg CC-90010 given once daily for 4 consecutive days on followed by 24 consecutive days off (4-days-on/24-days-off) in each 28-day cycle. A cohort s of up to approximately 20-25 subjects with relapsed and/or refractory DLBCL (Cohort 1) will be enrolled in Part B expansion.
Enrollment in advanced BCC (Cohort 2) will be stopped due to recruitment challenges. An additional cohort of approximately 15 evaluable subjects with R/R DLBCL (Cohort 3) will be enrolled under an alternative dosing regimen of 30 mg CC-90010 3days-on/11-days off in each 28-day cycle. The food effect assessment (Part C, Spain only) will evaluate the impact of food on CC-90010 when administered at the RP2D of 45 mg 4-days-on/24-days-off, by comparison of PK parameters following fasted and fed (high-fat, high-calorie meal) conditions in approximately 24 subjects with advanced solid tumors.
Follow-up Period:
In the Follow-up Period, subjects will be followed for 28 days (± 3 days) after the last dose of CC-90010 for safety.
After the Safety Follow-up visit, all subjects will be followed every subsequent 3 months (± 2 weeks) for survival follow-up for up until 2 years or until death, lost to follow-up, or the End of Trial, whichever occurs first.

STUDY DESIGN

Study Type:	Interventional
Estimated Enrollment :	140 participants
Intervention Model :	Single Group Assignment
Masking:	None (Open Label) ()
Primary Purpose:	Treatment
Official Title:	A Phase 1, Open-label, Dose-finding Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Efficacy of CC-90010 in Subjects With Advanced Solid Tumors and Relapsed/Refractory Non-Hodgkin's Lymphomas

Actual Study Start Date:	July 2017
Estimated Primary Completion Date:	August 2021
Estimated Study Completion Date:	August 2023

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: CC-90010 in patients with solid tumors and NHL Subjects will be administered orally once daily for 3 consecutive days followed by 4 consecutive days off drug every week (3/7-days schedule) in each 28 day cycle in Part A. Alternative dosing schedules (eg, 2-days-on/5-days- off each week, 3-days-on/4-days-off every other week, 4-days on/24 days off) may be evaluated one dosing schedule at a time or ≥ 2 dosing schedules given in parallel, based on the review of available safety, PK, pharmacodynamic (PD), and efficacy data.	Drug: CC-90010 CC-90010 is an oral, potent and reversible inhibitor of the epigenetic target bromodomain and extra-terminal (BET) proteins.

OUTCOME MEASURES

Primary Outcome Measures:
1. Adverse Events (AEs) [Time Frame: Up to 5 years]
Number of participants with adverse events
2. Dose Limiting Toxicities (DLTs) [Time Frame: Up to 5 years]
A DLT is defined as any of the toxicities described in the protocol occurring within the DLT assessment unless the event can clearly be determined to be unrelated to CC-90010
3. Maximum tolerated dose (MTD) [Time Frame: Up to 2 years]
The MTD is the highest dose that causes DLTs in not more than 33% of the subjects treated with CC-90010 in the first cycle with at least 6 evaluable subjects treated at this dose.

Secondary Outcome Measures:
1. Clinical benefit rate (CBR) [Time Frame: Up to 5 years]
Is defined as tumor responses (as assessed by the Investigators) of complete response (CR), partial response (PR) and stable disease (SD) (SD of ≥ 4 months duration).
2. Objective response rate (ORR) [Time Frame: Up to 5 years]
Is defined as the percent of subjects whose best response is CR or PR.
3. Duration of Response Rate [Time Frame: Up to 5 years]
Is measured from the time when criteria for CR/PR are first met (whichever is first recorded) until the first date at which progressive disease is objectively documented
4. Duration of stable disease [Time Frame: Up to 5 years]
For subjects with best response of SD, duration of SD is measured from the first dose date until the criteria for progression are met
5. Progression-free survival (PFS) [Time Frame: Up to 5 years]
Is defined as the time from the first dose of CC-90010 to the first occurrence of disease progression or death from any cause.
6. Overall survival [Time Frame: Up to 5 years]
Is measured as the time from the first dose of CC-90010 to death due to any cause.
7. Pharmacokinetic- Cmax [Time Frame: Up to 5 years]
Maximum observed plasma concentration on first and last day of dosing within a cycle
8. Pharmacokinetic- AUC [Time Frame: Up to 5 years]
Area under the plasma concentration time-curve on first and last day of dosing within a cycle
9. Pharmacokinetic- Tmax [Time Frame: Up to 5 years]
Time to maximum plasma concentration on first and last day of dosing within a cycle
10. Pharmacokinetic- t1/2 [Time Frame: Up to 5 years]
Terminal half-life on last day of dosing within a cycle
11. Apparent Clearance [Time Frame: Up to 5 years]
Apparent total systemic clearance to be estimated following the last dose in cycle 1
12. Apparent Volume of Distribution [Time Frame: Up to 5 years]
Apparent steady state volume of distribution to be estimated following the last dose in cycle 1
13. Pharmacokinetic- AUClast [Time Frame: Up to 5 years]
Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration
14. Pharmacokinetic- AUC0-24 [Time Frame: Up to 5 years]
Area under the plasma concentration-time curve calculated from time zero to 24 hours
15. Pharmacokinetic- AUC0-∞ [Time Frame: Up to 5 years]
Area under the concentration-time curve calculated from time zero to infinity

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. Age = or > 18 years.
2. For subjects enrolling in food-effect assessment (Part C) only: a. Subject must agree and be willing to consume a standard high-fat, high-calorie meal. b. Subject must be willing to refrain from caffeine or xanthene-containing products (coffee, tea, cola, chocolate, etc.) for 48 hours prior to dosing on Cycle 1 Day 4 and Cycle 2 Day 4 and up to 24 hours post dose.
3. Subjects with histological or cytological confirmation of either:
1. In Part A, advanced or unresectable solid tumors or advanced relapsed and/or refractory Non-Hodgkin lymphoma (ie, Diffuse large B-cell lymphoma and Follicular lymphoma or Marginal zone lymphoma) including those who have progressed on (or not been able to tolerate due to medical comorbidities or unacceptable toxicity) standard anticancer therapy or for whom no other approved conventional therapy exists.
2. In Part B dose expansion, - Cohorts 1 and 3: relapsed and/or refractory DLBCL following at least 2 prior lines of therapy (e.g. have failed at least one line of standard therapy and have received at least one prior line of salvage therapy) OR have failed at least one prior line of standard therapy and are not eligible for autologous stem cell transplant (ASCT) or have declined ASCT; transformed lymphoma following chemotherapy for lower grade lymphoma and at least two standard treatment regimen for DLBCL.
Subjects with two or more lines of systemic therapy must have been treated with and have lack of response after chimeric antigen receptor (CAR) T-cell therapy, if such therapy is available, OR be ineligible for CAR T-cell therapy at the time of enrollment, OR subject declined CAR T-cell therapy.
- Cohort 2: advanced basal cell carcinoma including those who have progressed on (or not been able to tolerate due to medicalcomorbidities or unacceptable toxicity) standard anticancer therapy or for whom no other approved conventional therapy exists.
In Part C, advanced or unresectable solid tumors including those who have progressed on (or not been able to tolerate due to medical comorbidities or unacceptable toxicity) standard anticancer therapy or for whom no other approved conventional therapy exist
4. At least one site of measurable disease for subjects with solid tumors; bi-dimensionally measurable disease on cross sectional imaging with at least one lesion >1.5 cm for subjects with NHL. For subjects with rare malignancies evaluable disease can be considered.
5. Tumor biopsies whenever safe and feasible will be collected in Part A, except for subjects with GBM. Subject consents to mandatory tumor biopsies (Screening and on treatment) in Part B. In exceptional circumstances an exemption waiver may be granted by the Sponsor for this criterion
6. ECOG PS of 0 to 1.
7. Either commit to true abstinence or agree to use effective contraceptive methods and follow pregnancy precautions
Exclusion Criteria:
Principal Exclusion Criteria
1. Subject has received anti-cancer therapy (either approved or investigational) within <or= 4 weeks or 5 half-lives, whichever is shorter prior to starting CC-90010. 2. Subject has received prior CAR T-cell therapy or other T-cell targeting treatment (approved or investigational) ≤ 4 weeks prior to starting CC-90010. 3. Toxicities resulting from prior systemic cancer therapies must have resolved. to ≤ NCI CTCAE Grade 1 prior to starting CC-90010 treatment 4. Subject has received autologous hematologic stem cell transplant (HSCT) <or= 3 months prior to starting CC-90010 treatment. Subjects with allogeneic HSCT will not be allowed on this protocol. 5. Major surgery <or= 4 weeks or minor surgery <or= 2 weeks prior to starting CC-90010 or subjects who have not recovered from surgery. 6. Completed radiation treatment < 4 weeks prior to starting CC-90010. 7. Symptomatic, untreated, or unstable central nervous system (CNS) metastases. 8. Known symptomatic acute or chronic pancreatitis. 9. Impaired cardiac function or clinically significant cardiac diseases. 10. Pregnant or nursing females. 12. History of concurrent second cancers requiring active, ongoing systemic treatment. 13. History of clinically significant cognitive disorder(s) or active cognitive disorder(s). 13. Evidence of history of bleeding diathesis. 14. Subjects with known prior episodes of non-arteritic anterior ischemic optic neuropathy (NAION) should be excluded from the study. CC-90010 should be used with caution in subjects with retinitis pigmentosa 15. Any significant medical condition that would prevent the subject from participating (or compromise compliance) in the study or would place the subject at unacceptable risk if he/she were to participate in the study. 16. Patients with poor bone marrow reserve as assessed by the Investigator such as in the following conditions: - Having received extensive bone radiotherapy - Having experienced several episodes of bone marrow aplasia in previous treatments - Confirmed histological bone marrow cancer infiltration (with exemption of NHL) - Requiring regular hematopoietic support (blood transfusion, erythropoietin, GCSF)

CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

France	Institut Bergonie Centre Regional de Lutte Contre Le Cancer de Bordeaux Et Sud Ouest	Bordeaux
France	Gustave Roussy - Cancer Campus	Villejuif
Italy	Istituto Scientifico Romagnolo Per Lo Studio e La Cura Dei Tumori (I.R.S.T.)	Meldola
Italy	Istituto Nazionale Per Lo Studio E La Cura Dei Tumori Fondazione Giovanni Pascale	Napoli, Campania
Italy	Istituto Clinico Humanitas	Rozzano (MI)
Japan	Aichi Cancer Center Hospital	Chikusa-ku
Japan	National Cancer Center Hospital East	Kashiwa
Japan	The Cancer Institute Hospital of Japanese Foundation For Cancer Research	Koto-ku
Spain	Hospital Val d'Hebron	Barcelona
Spain	Hospital Universitario Fundacion Jimenez Diaz	Madrid
Spain	Hospital 12 de Octubre	Madrid

Sponsors and Collaborators

Celgene

Investigator

Study Director : Zariana Nikolova, MD, PhD Celgene

MORE INFORMATION

Responsible Party :	Celgene
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Other Study ID Numbers :	CC-90010-ST-001, U1111-1194-8570, 2015-004371-79
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Plan to Share IPD:	No
Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
Product Manufactured in and Exported from the U.S.:	Yes
Keywords provided by Celgene:	*Safety* *Efficacy* *CC-90010 Non-Hodgkin's Lymphomas* *Solid Tumors* *Relapsed/Refractory*
Additional relevant MeSH terms :	*Lymphoma* *Lymphoma, Non-Hodgkin*