A Safety and Efficacy Study of CC-90011 in Subjects With Relapsed and/or Refractory Solid Tumors and Non-Hodgkin's Lymphomas

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT02875223	RECRUITING	AUGUST 23, 2016	OCTOBER 1, 2020

STUDY DESCRIPTION

Brief Summary

Study CC-90011-ST-001 is an open-label, Phase 1, dose escalation and expansion, First-In-Human (FIH) clinical study of CC-90011 in subjects with advanced unresectable solid tumors (enriched for grade 2 NENs, grade 2 NETs and NECs) and R/R NHL (MZL, including transformed MZL). The dose escalation part (Part A) of the study will explore escalating oral doses of CC-90011 to estimate the maximum tolerated dose (MTD) of CC-90011. The expansion part (Part B) will further evaluate the safety and efficacy of CC-90011 administered at or below the MTD in 3 selected expansion cohorts of approximately 10-20 evaluable subjects each, in order to further define the RP2D.

Condition or Disease: Neoplasms
Lymphoma, Non-Hodgkin

Intervention/treatment: Drug: CC-90011

Phase: Phase 1

DETAILED DESCRIPTION

Parts A and B 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-90011. The informed consent form (ICF) 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-90011.
Treatment Period During the Treatment Period, CC-90011 will initially be administered orally in each 4-week (28 day) Cycle in Part A.
In September 2018, after completion of Part A, the SRC determined the RP2D to be 60 mg CC 90011 once weekly (QW) in each 28-day cycle. In Part B, 3 cohorts, of approximately 10-20 evaluable subjects each, with advanced low/intermediate-grade lung NETs, NEPCs, R/R NHL (MZL, including transformed MZL) will receive the RP2D to further evaluate safety, PK, PD and preliminary efficacy.
Follow-up Period In the Follow-up Period, subjects will be followed for 28 days (± 3 days) after the last dose of CC-90011 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 : 76 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, Pharmacokinetic and Preliminary Efficacy of CC-90011 in Subjects With Advanced Solid Tumors and Non-Hodgkin Lymphomas

Actual Study Start Date: August 2016

Estimated Primary Completion Date: June 2021

Estimated Study Completion Date: September 2023

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: CC-90011 Administration Subjects will administer CC-90011 orally once weekly in each 4 -week (28 day) Cycle. Alternative dosing schedules may be implemented based on the review of clinical safety and laboratory data by the SRC. CC-90011 will be administered with at least 240 mL of water. Subjects should fast for a minimum of 4 hours in both Parts A and B prior to CC-90011 administration and refrain from any food intake for up to 1 hour after dosing	Drug: CC-90011

OUTCOME MEASURES

Primary Outcome Measures: 1. Dose-Limiting Toxicity (DLT) [Time Frame: Up to approximately 28 days]
Number of participants with DLT

	2. Adverse Events (AEs) [Time Frame: Up to 6 years] Number of participants with adverse events
Secondary Outcome Measures:	1. Clinical Benefit Rate (CBR) [Time Frame: Up to 6 years] Is defined as tumor responses (as assessed by the Investigators) of complete response (CR), partial response (PR) and durable stable disease (SD) (SD of ≥ 4 months duration). 2. Objective Response Rate (ORR) [Time Frame: Up to 6 years] Is defined as the percent of subjects whose best response is complete response (CR) or partial response (PR). 3. Progression-Free Survival (PFS) [Time Frame: Up to 6 years] Is defined as the time from the first dose of CC-90011 to the first occurrence of disease progression or death from any cause. 4. Overall Survival (OS) [Time Frame: Up to 6 years] Is measured as the time from the first dose of CC-90011 to death due to any cause. 5. Pharmacokinetics - Cmax [Time Frame: Up to 6 years] Maximum observed plasma concentration 6. Pharmacokinetics - AUC [Time Frame: Up to 6 years] Area under the plasma concentration time-curve 7. Pharmacokinetics -Tmax [Time Frame: Up to 6 years] Time to maximum plasma concentration 8. Pharmacokinetics -t1/2 [Time Frame: Up to 6 years] Terminal half-life 9. Pharmacokinetics -CL/F [Time Frame: Up to 6 years] Apparent total body clearance 10. Pharmacokinetics -Vz/F [Time Frame: Up to 6 years] Apparent volume of distribution

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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:
Subjects must satisfy the following criteria to be enrolled in the study:
1. ≥ 18 years of age
2. Part A:
- Subjects with histological or cytological confirmation of advanced unresectable solid tumors (including Grade 2 neuroendocrine neoplasms (NENs)/ neuroendocrine tumors (NETs), small cell lung cancer (SCLC), and other neuroendocrine carcinomas (NECs)) or R/R Non-Hodgkin's lymphomas (NHL) (diffuse large B cell lymphoma (DLBCL) and follicular lymphoma (FL) or marginal cell lymphoma MZL))
3. Absolute neutrophil count (ANC) ≥ 1.5 x 109/L without growth factor support for 7 days (14 days if subject received pegfilgastrim)
4. Hemoglobin (Hgb) ≥ 10 g/dL (≥ 100 g/L or > 6.2 mmol/L)
5. Platelet Count
- Platelet count (plt) ≥ 100 x 109/L (≥ 50 x 109/L for NHL subjects) or ≥ 75 x 109/L for HCC or NEHCC subjects with portal hypertension without transfusion for 7 days (Part A).
- Platelet count (plt) ≥ 150 x 109/L (Part B, solid tumor cohort in particular NET and CRPC).
- Platelet count (plt) ≥ 50 x 109/L (Part B, NHL cohort)
6. Part B:
Neuroendocrine tumors: Subjects with histological or cytological confirmation of advanced unresectable solid tumors (including low/intermediate-grade lung NETs, and Prostrate NECs (NEPCs)) which fall under one of the following categories:
B) Lung NETs:
Subjects with demonstrated tumor progression in the last 12 months on last prior therapy assessed by CT/MRI scan in the following 2 histologies.
i. Typical carcinoid (TC) ii. Atypical carcinoid (AC)
C) Prostate NECs (NEPCs):
1. Appropriate pathological features according to WHO classification
2. Expression of neuroendocrine markers
3. Mitotic count ≥ 2 -10 per 10 HPF or ≥ 2-10 per 2mm2 and/or ≥ 3% Ki67 index (if reliably available)
D) R/R NHL:
Subjects with MZL, including histologic transformation of MZL relapsed/refractory after ≥2 prior therapies and ineligible for potentially curative therapy with the adequate immunohistochemistry markers.
Subjects must have progressed on (or not been able to tolerate due to medical comorbidities or unacceptable toxicity), or following standard anticancer therapy or for whom no other approved conventional therapy exists or is acceptable
Exclusion Criteria:
The presence of any of the following will exclude a subject from enrollment:
1. low grade (G1) neuroendocrine tumors (<2 per high power fields (HPF) or < 2 per mm2 and/or ≤ 2% Ki67 index) such as carcinoid are excluded. 2. Subject has received anti-cancer therapy (either approved or investigational) ≤ 4 weeks or 5 half-lives, whichever is shorter, prior to Cycle 1 Day 1.. - < 42 days for prior nitrosureas or mitomycin C 3. Toxicities resulting from prior systemic cancer therapies must have resolved to ≤National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Grade 1 prior to starting CC-90011 treatment (with exception of grade 2 peripheral neuropathy and alopecia). 4. Prior autologous stem cell transplant ≤ 3 months before first dose or those who have not recovered. 5. Prior allogeneic stem cell transplant with either standard or reduced intensity conditioning. 6. Subject has undergone major surgery ≤ 4 weeks or minor surgery ≤ 2 weeks prior to Cycle 1 Day 1 or who have not recovered from surgery. 7. Subject has completed any radiation treatment < 4 weeks prior to Cycle 1 Day 1 or 25% of myelopoetic BM radiation are not allowed to be enrolled on this study.
8. Subject has persistent diarrhea due to a malabsorptive syndrome (such as celiac sprue or inflammatory bowel disease) ≥ NCI CTCAE Grade 2, despite medical management), or any other significant GI disorder that could affect the absorption of CC-90011.
9. Subject with symptomatic or uncontrolled ulcers (gastric or duodenal), particularly those with a history of and/or risk of perforation and GI tract hemorrhages.
10. Subject with any hemorrhage/bleeding event > CTCAE Grade 2 or haemoptysis > 1 teaspoon within 4 weeks prior to the first dose
11. Symptomatic and untreated or unstable central nervous system (CNS) metastases as per protocol.
12. Subject with SCLC that has history of interstitial lung disease (ILD) OR a history of pneumonitis that has required oral or Intra Venous (IV) steroids
13. Subject has known symptomatic acute or chronic pancreatitis.
14. Subject has impaired cardiac function or clinically significant cardiac diseases, as per protocol.
15. Subject has other clinically significant heart disease such as congestive heart failure requiring treatment or uncontrolled hypertension (blood pressure ≥ 160/95 mm Hg).
16. Subject is a pregnant or nursing female.
17. Subject has known Human immunodeficiency virus (HIV) infection.
18. Subject has known chronic active hepatitis B or C virus (HBV, HCV) infection.
19. Subject with ongoing treatment with chronic, therapeutic dosing of anti-coagulants (eg, warfarin, low molecular weight heparin, Factor Xa inhibitors, thrombin antagonist). Low dose low molecular weight heparin for catheter maintenance and for short-term prophylaxis for subjects with prior PE and DVT are permitted under careful consideration by the Investigator.
20. Subject has a history of concurrent second cancers requiring active, ongoing systemic treatment.
21. Subject has any significant medical condition (eg, active or uncontrolled infection or renal disease), laboratory abnormality, or psychiatric illness 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.
22. Subjects with poor bone marrow reserve as assessed by Investigator such as in the following conditions of (Part B only):
- Having received extensive bone radiotherapy
- Having experienced several episodes of bone marrow aplasia in previous treatments
- Confirmed histological bone marrow cancer infiltration
- Requiring regular hematopoietic support (blood transfusion, erythropoietin, GCSF).)
23. Subject has any condition that confounds the ability to interpret data from the study.

CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

France	Centre Georges Francois Leclerc	Dijon
France	Institut Paoli Calmettes	Marseille Cedex 9

France	Gustave Roussy	Villejuif Cedex
Italy	Bologna University	Bologna
Italy	Istituto Nazionale Dei Tumori	Milano
Italy	Istituto Europeo di Oncologia	Milano
Spain	Hospital Universitario Vall D hebron	Barcelona
Spain	Fundacion Jimenez Daaz	Madrid
Spain	Hospital Universitario Marques de Valdecilla	Santander
United Kingdom	Royal Marsden Hospital	London
United Kingdom	Freeman Hospital	Newcastle Upon Tyne

Sponsors and Collaborators

Celgene

Investigator

Study Director :	Zariana Nikolova, MD, PhD	Celgene Corporation
Principal Investigator :	Johann De Bono, MD, PhD	Royal Marsden NHS Foundation Trust
Principal Investigator :	Antoine Hollebecque, MD	Gustave Roussy, Cancer Campus, Grand Paris

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MORE INFORMATION

Responsible Party :	Celgene
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Keywords provided by Celgene:	*Safety* *CC-90011* *Advanced unresectable solid Tumors Low intermediate-grade lung neuroendocrine tumors (Typical and Atypical carcinoids)* *Neuroendocrine prostate cancer (NEPC)* *R/R Non-Hodgkin's Lymphomas*
Additional relevant MeSH terms :	*Lymphoma* *Lymphoma, Non-Hodgkin*