A Safety, Tolerability and Preliminary Efficacy Evaluation of CC-90011 Given in Combination With Cisplatin and Etoposide in Subjects With First Line, Extensive Stage Small Cell Lung Cancer

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT03850067	RECRUITING	FEBRUARY 21, 2019	AUGUST 31, 2020

STUDY DESCRIPTION

Brief Summary

CC-90011-SCLC-001 is a multicenter, Phase 1b, open-label, dose finding study to assess the safety, tolerability, and preliminary efficacy of CC-90011 given concurrently and sequentially to standard of care platinum-based, cisplatin and etoposide, carboplatin and etoposide and/or etoposide and Nivolumab to subjects with first line ES SCLC. The dose finding part of the study will explore escalating oral doses of CC-90011 in combination with cisplatin, etoposide and/or carboplatin with or without Nivolumab (chemotherapy), to determine the maximum tolerated dose of CC- 90011 in combination with chemotherapy with or without Nivolumab to subjects with first line ES SCLC.

Condition or Disease: Small Cell Lung Carcinoma

Intervention/treatment: Drug: CC-90011
Drug: Cisplatin
Drug: Carboplatin
Drug: Etoposide
Drug: Nivolumab

Phase: Phase 1/Phase 2

DETAILED DESCRIPTION

N/A

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 90 participants

Intervention Model : Single Group Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Phase 1b, Multicenter, Open-label, Dose Finding Study to Assess the Safety, Tolerability, and Preliminary Efficacy of CC-90011 Given in Combination With Cisplatin and Etoposide in First -Line, Extensive Stage Subjects With Small Cell Lung Cancer

Actual Study Start Date: March 2019

Estimated Primary Completion Date: September 2021

Estimated Study Completion Date: December 2022

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: CC-90011 in combination with Cisplatin and Etoposide During the Chemotherapy Treatment Period, the dose escalation is designed to explore three dose levels of CC-90011, for example 20, 40, and 60 mg as determined by Bayesian design, administered orally Days 1 and 8, in combination with cisplatin intravenous (IV) 75 mg/m2, Day 1, and etoposide iv 100 mg/m2 on Days 1, 2, and 3, for 4 cycles of 21 days each. Subjects completing the chemotherapy and being responders as per RECIST 1.1 will enter the Maintenance Treatment Period. Subjects completing 6 cycles of maintenance treatment subject will be treated only with CC-90011 at RP2D (60 mg) and continuing on CC-90011 are only required to have clinic visits/assessments performed on Day 1 (± 3 days) of each subsequent cycle (Cycles 6 and higher) unless more frequent visits are clinically indicated.	Drug: CC-90011 CC-90011 Drug: Cisplatin Cisplatin
Experimental: CC-90011 in combination with Carboplatin and Etoposide During the Chemotherapy Treatment Period, the dose escalation is designed to explore three dose levels of CC-90011, for example 20, 40, and 60 mg as determined by Bayesian design, administered orally Days 1 and 8, in combination with cisplatin intravenous (IV) 75 mg/m2, Day 1, and etoposide iv 100 mg/m2 on Days 1, 2, and 3, for 4 cycles of 21 days each. Subjects completing the chemotherapy and being responders as per RECIST 1.1 will enter the Maintenance Treatment Period. Subjects completing 6 cycles of maintenance treatment subject will be treated only with CC-90011 at RP2D (60 mg) and continuing on CC-90011 are only required to have clinic visits/assessments performed on Day 1 (± 3 days) of each subsequent cycle (Cycles 6 and higher) unless more frequent visits are clinically indicated	Drug: Carboplatin Carboplatin Drug: Etoposide Etoposide

Experimental: Nivolumab combination When the RP2D of CC-90011 in combination with cisplatin or carboplatin and etoposide is determined, the combination of CC-90011 at RP2D with cisplatin or carboplatin and etoposide plus nivolumab (Nivo) IV 240 mg Day 1 of each chemotherapy cycle, will be explored. For CC-90011 in combination with chemotherapy and Nivo, the starting dose will be the RP2D of CC-90011 in combination with chemotherapy. For subjects responding to the initial combination of CC-90011 and chemotherapy, as per RECIST 1.1, CC-90011 single agent will be given as maintenance therapy. These subjects will receive 60 mg of CC-90011 orally once weekly, Days 1, 8, 15, and 22, during cycles of 28 days each. For subjects responding to the initial combination of CC-90011 and chemotherapy with Nivo, CC-90011 with Nivo will be given as maintenance therapy. These subjects will receive 60 mg of CC-90011 orally once weekly, Days 1, 8, 15, and 22, and Nivo IV 240 mg Days 1 and 15 during cycles of 28 days each	Drug: Nivolumab Nivolumab

OUTCOME MEASURES

Primary Outcome Measures:	1. Dose-Limiting Toxicity (DLT) [Time Frame: Up to approximately 2 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-90011 2. Maximum Tolerated Dose (MTD) [Time Frame: Up to approximately 2 years] 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 3. Adverse Events (AEs) [Time Frame: Up to approximately 3 years] 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. Objective Response Rate (ORR) [Time Frame: Up to approximately 2 years] Is defined as the percent of subjects whose best response is complete response (CR) or partial response (PR). 2. Progression-free Survival (PFS) [Time Frame: Up to approximately 2 years] Is defined as the time from the first dose of study drug to the first occurrence of disease progression or death from any cause. 3. Overall Survival (OS) [Time Frame: Up to approximately 2 years] Is measured as the time from the first dose of CC-90011 to death due to any cause. 4. Pharmacokinetics- Cmax [Time Frame: Up to approximately 2 years] Maximum observed plasma concentration 5. Pharmacokinetics- AUC [Time Frame: Up to approximately 2 years] Area under the plasma concentration time-curve 6. Pharmacokinetics- Tmax [Time Frame: Up to approximately 2 years] Time to maximum plasma concentration 7. Pharmacokinetics- t1/2 [Time Frame: Up to approximately 2 years] Terminal half-life 8. Pharmacokinetics- CL/F [Time Frame: Up to approximately 2 years] Apparent clearance 9. Pharmacokinetics- VzF [Time Frame: Up to approximately 2 years] Apparent volume of distribution

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. Male and female subject is 18 years of age or older at the time of signing the informed consent form (ICF).
2. Subject with histological or cytological confirmation of extensive stage SCLC according to 2015 WHO classification (Travis, 2015).
3. Subject must be able to provide fresh or archival tumor tissues
4. Subject is found suitable for at least 4 cycles of platinum-based standard chemotherapy.
5. Subject has at least 1 site of measurable disease per RECIST 1.1.
6. Subject must have the following laboratory values:
- Absolute neutrophil count (ANC) ≥ 1.5 x 109/L
- Hemoglobin (Hgb) ≥ 10 g/dL (≥ 100 g/L or > 6.2 mmol/L)
- Platelet count (Plt) ≥ 150 x 109/L
- Serum aspartate aminotransferase/serum glutamic oxaloacetic transaminase (AST/SGOT) and alanine aminotransferase/serum glutamate pyruvate transaminase (ALT/SGPT) ≤ 3.0 x upper limit of normal (ULN) or ≤ 5.0 x ULN if liver metastases are present
- Serum total bilirubin ≤ 1.5 x ULN
- Serum albumin ≥ 3.0 g/dL
- Serum creatinine ≤ 1.5 mg/dL or creatinine clearance ≥ 60 mL/min (see Appendix G to see creatinine clearance formula). For the purposes of this protocol, the glomerular filtration rate (GFR) is considered to be equivalent to the creatinine clearance.
- Prothrombin time (or international normalized ratio [INR]) and activated partial thromboplastin time (APTT) ≤ 1.5 ULN
Exclusion Criteria:
1. Subject has received anticancer therapy (either approved or investigational, including radiation with curative intent) for SCLC prior to study entry.
2. Subject has undergone major surgery ≤ 4 weeks prior to Cycle 1 Day 1 or has not recovered from surgery.
3. 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 gastrointestinal (GI) disorder that could affect the absorption of CC- 90011.
4. Subject with symptomatic or uncontrolled ulcers (gastric or duodenal), particularly those with a history of and/or risk of perforation and GI tract hemorrhages.
5. Subject with any hemorrhage/bleeding event > CTCAE Grade 2 or hemoptysis > 1 teaspoon within 4 weeks prior to the first dose.
6. Subject with symptomatic and untreated or unstable central nervous system (CNS) metastases.
7. Subject has impaired cardiac function or clinically significant cardiac diseases, including any of the following:
- Left ventricular ejection fraction (LVEF) 10 mg daily prednisone equivalent) or other immunosuppressive medications within 30 days of enrollment. Inhaled or topical steroids, and adrenal replacement steroid doses > 10 mg daily prednisone equivalent, are permitted in the absence of active autoimmune disease.
• Subjects with type 1 diabetes mellitus, hypothyroidism only requiring hormone replacement, disorders (such as vitiligo, psoriasis, or alopecia) not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger are permitted to enroll.
22. Subject has received treatment with botanical preparations (eg, herbal supplements or traditional Chinese medicines) to treat the disease under study within 2 weeks prior to randomization. Refer to Section 8.2 for prohibited therapies.
23. Subject has history of allergy or hypersensitivity to study drug components.
24. Subject has received a live/attenuated vaccine within 30 days of first treatment.

CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

France	Hospital Le Timone	Marseille Cedex 5
France	CHU Nantes Hopital Nord Laennec	Saint-Herblain
France	Gustave Roussy	Villejuif CEDEX
Italy	Azienda Ospedaliero Universitaria Ospedali Riuniti "Umberto I, G.M. Lancisi, G. Salesi"	Ancona
Italy	Polyclinic S. Orsola-Malpighi	Bologna
Italy	Istituto Clinico Humanitas	Rozzano (MI)
Spain	Vall d´Hebron University Hospital	Barcelona
Spain	Hospital Universitario Germans Trias i Pujol	Barcelona
Spain	Hospital Doce de Octubre	Madrid
Spain	Hospital Universitario Puerta de Hierro	Majadahonda, Madrid
Spain	Hospital Universitario Virgen de la Victoria	Malaga
Spain	Hospital Clinico Universitario de Valencia	Valencia
Spain	Hospital Universitario La Fe	Valencia

Sponsors and Collaborators

Celgene

Investigator

Study Director :	Zariana Nikolova, MD, PHD	Celgene Corporation
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Principal Investigator :	Benjamin Besse, MD, PhD	Gustave Roussy, Ditep

MORE INFORMATION

Responsible Party :	Celgene
ClinicalTrials.gov Identifier :	NCT03850067
Other Study ID Numbers :	CC-90011-SCLC-001, U1111-1228-2067, 2018-002799-42
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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:	No
Studies a U.S. FDA-regulated Device Product:	No
Keywords provided by Celgene:	*Safety* *CC-90011 Extensive stage small cell lung cancer*
Additional relevant MeSH terms :	*Lung Neoplasms* *Small Cell Lung Carcinoma*