# A Safety and Efficacy Study of CC-90011 in Combination With Nivolumab in Subjects With Advanced Cancers

| CLINICALTRIALS.GOV IDENTIFIER | RECRUITMENT STATUS | FIRST POSTED | LAST UPDATE POSTED |
|---|---|---|---|
| NCT04350463 | RECRUITING | APRIL 17, 2020 | OCTOBER 2, 2020 |

## STUDY DESCRIPTION

### Brief Summary

This is a Phase 2, multicenter, open-label, multi-cohort study to assess safety and efficacy of CC-90011 in combination with nivolumab in subjects with small cell lung cancer or squamous non-small cell lung cancer who have progressed after 1 or 2 lines of therapies. The primary objectives of the study are to evaluate the overall response rate of subjects treated with CC-90011 in combination with nivolumab in three cohorts: - Cohort A: SCLC in ICI naïve subjects - Cohort B: SCLC in ICI progressor subjects - Cohort C: sqNSCLC in ICI progressor subjects Overall response rate is defined as the proportion of subjects in the treated population who had complete response (CR) or partial response (PR) as assessed by Investigator review per RECIST v1.1. In Cohort A, expected ORR for nivolumab monotherapy is 14% while target ORR is 30%. To achieve at least 80% power with one-sided type 1 error 0.1, 39 subjects will be enrolled according to a 2-stage group sequential design based on a binomial test. In stage 1, 12 subjects will be enrolled and treated with CC-90011 in combination with nivolumab. If there are 2 or more subjects responding, Cohort A will continue to enroll an additional 27 subjects. If 1 or less subjects respond in stage 1, Cohort A will stop for futility. In Cohort B and C, expected ORR for nivolumab monotherapy is 5% while target ORR is 15%. To achieve at least 80% power with one-sided type 1 error 0.1, 48 subjects will be enrolled according to a 2-stage group sequential design based on a binomial test. In stage 1, 14 subjects will be enrolled and treated with CC-90011 in combination with nivolumab. If there are 1 or more subjects responding, Cohort B and C will continue to enroll an additional 34 subjects each. If 0 subjects respond in stage 1, Cohort B and C will stop for futility.

**Condition or Disease:** Neoplasms

**Intervention/treatment:** Drug: CC-90011
Drug: Nivolumab

**Phase:** Phase 2

## DETAILED DESCRIPTION

N/A

## STUDY DESIGN

**Study Type:** Interventional

**Estimated Enrollment :** 135 participants

**Intervention Model :** Parallel Assignment

**Masking:** None (Open Label) ()

**Primary Purpose:** Treatment

**Official Title:** A Phase 2, Multicenter, Open-label, Multi-cohort Study to Assess Safety and Efficacy of CC-90011 in Combination With Checkpoint Inhibitor(s) in Subjects With Advanced Cancers

**Actual Study Start Date:** July 2020

**Estimated Primary Completion Date:** December 2022

**Estimated Study Completion Date:** September 2024

## ARMS AND INTERVENTIONS

| Arm | Intervention/treatment |
|---|---|
| Experimental: Arm A: SCLC in ICI naïve subjects<br>CC-90011 will be given orally (PO) at a dose of 60 mg on a once weekly basis in a continuous 28-day cycle. Nivolumab will be administered intravenously at a dose of 480 mg every 4 weeks per local practice as a 30 minute or a 60-minute infusion as per local practice. | Drug: CC-90011<br>CC-90011<br><br>Drug: Nivolumab<br>Nivolumab |
| Experimental: Cohort B: SCLC in ICI progressor subjects<br>CC-90011 will be given orally (PO) at a dose of 60 mg on a once weekly basis in a continuous 28-day cycle. Nivolumab will be administered intravenously at a dose of 480 mg every 4 weeks per local practice as a 30 minute or a 60-minute infusion as per local practice. | Drug: CC-90011<br>CC-90011<br><br>Drug: Nivolumab<br>Nivolumab |
| Experimental: Cohort C: sqNSCLC in ICI progressor subjects<br>CC-90011 will be given orally (PO) at a dose of 60 mg on a once weekly basis in a continuous 28-day cycle. Nivolumab will be administered intravenously at a dose of 480 mg every 4 weeks per local practice as a 30 minute or a 60-minute infusion as per local practice.: | Drug: CC-90011<br>CC-90011<br><br>Drug: Nivolumab<br>Nivolumab |

## OUTCOME MEASURES

Primary Outcome Measures: 1. Overall response rate [ Time Frame: Up to 24 months ]
The proportion of subjects in the treated population who had complete response (CR) or partial response (PR) as assessed by Investigator review per RECIST v1.1

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| Secondary Outcome Measures: | 1. Adverse Events (AEs) [ Time Frame: Up to 24 months ]<br>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. All adverse events will be collected and collated according to grade and frequency. This will include all events considered related or unrelated to study therapy.<br>2. Duration of response [ Time Frame: Up to 24 months ]<br>Every 6 weeks post C1D1 for the first 24 weeks and then every 8 weeks until disease progression, new anticancer therapy, death or withdrawal by subject.<br>3. Progression-free survival [ Time Frame: Up to 24 months ]<br>The time from the first dose of the study drug to the date of the first objectively documented tumor progression as assessed by Investigator review per RECIST v1.1 or death from any cause, whichever occurs first.<br>4. Overall Survival [ Time Frame: Up to 48 months ]<br>The time from the first dose of the study drug to the date of death due to any cause. |

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**ELIGIBILITY CRITERIA**

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| **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. Subject is ≥ 18 years of age at the time of signing the informed consent form (ICF).
2. Subject with histological or cytological confirmation of extensive stage Small Cell Lung Cancer (ES SCLC) or Stage IIIb or IV squamous Non-Small Cell Lung Cancer (sqNSCLC)
3. Subject has received 1 or 2 prior lines of therapies, defined as:
1. Cohort A (SCLC, Immune Checkpoint Inhibitor naïve):
- At least 1 prior treatment including a platinum-based chemotherapy doublet
- A minimum of 3 cycles of platinum-based chemotherapy in first line treatment, unless stopped at 2 cycles due to treatment-related toxicity
2. Cohort B (SCLC, ICI progressors):
- At least 1 prior first or second line treatment includes an ICI
- If treatment includes an ICI as maintenance therapy, at least 1 cycle of ICI in maintenance should have been completed
- At least 1 prior treatment including a platinum-based chemotherapy doublet
- A minimum of 3 cycles of platinum-based chemotherapy, with or without ICI, in first line treatment, unless stopped at 2 cycles due to treatment-related toxicity
- Subject must have progressed during ICI therapy, defined as unequivocal progression on or within 3 months of the last dose of ICI therapy (if no subsequent therapy)
3. Cohort C (sqNSCLC, ICI progressors):
- At least 1 prior first or second line treatment includes an ICI
- If treatment includes an ICI as maintenance therapy, at least 1 cycle of ICI in maintenance should have been completed
- At least 1 prior treatment including a platinum-based chemotherapy doublet
- A minimum of 3 cycles of platinum-based chemotherapy, with or without an ICI, in first line treatment, unless stopped at 2 cycles due to treatment-related toxicity
- Subject must have progressed during ICI therapy, defined as unequivocal progression on or within 3 months of the last dose of ICI therapy (if no subsequent therapy)
4. Subject has progressed at the last line of therapy.
5. Subject has a measurable disease defined by RECIST v1.1.
6. Subject agrees to provide a tumor biopsy from primary or metastatic site prior to first dose and at a pre-specified timepoint during treatment. Core biopsy is required however, in the event a core biopsy may not otherwise be feasible in the opinion of the treating physician, an endobronchial ultrasound-guided fine needle aspirate [EBUS-FNA]) biopsy, using the largest gauge needle, may be performed instead.
7. Subject has ECOG Performance Status of 0 to 1.
8. Subject must have the following laboratory values:
1. Absolute neutrophil count (ANC) ≥ 1.5 x 109/L
2. Hemoglobin (Hgb) ≥ 9 g/dL (one-time blood transfusion is allowed)
3. Platelet (Plt) Count ≥ 150 x 109/L
4. White blood cells (WBC) ≥ 2 x 109L
5. Serum AST/serum glutamic oxaloacetic transaminase (SGOT) or ALT/serum glutamic pyruvic transaminase (SGPT) ≤ 3 x upper limit of normal (ULN) or ≤ 5 x ULN if presence of liver metastases
6. Total serum bilirubin ≤ 1.5 x ULN (≤ 3 x ULN, if Gilbert's syndrome or if indirect bilirubin concentrations are suggestive of extrahepatic source of the elevation)
7. Creatinine clearance (CrCl) ≥ 60 mL/minute based on Cockcroft-Gault or modification of diet in renal disease (MDRD) or ≥ 60 mL/min/1.73 m2
Exclusion Criteria:
The presence of any of the following will exclude a subject from enrollment:
1. Subject has not recovered to Grade 2 or lower clinically significant toxicities related to the prior therapy (alopecia excluded).
2. Subject has received prior LSD1 therapies.
3. Subject has a history of severe hypersensitivity reactions to other monoclonal antibodies
4. Subject with symptomatic and untreated or unstable central nervous system (CNS) metastases.
1. Subject has recently been treated with whole brain radiation or stereotactic radiosurgery for CNS metastases must have completed therapy at least 2 weeks prior to Cycle 1 Day 1 and has a follow-up brain computed tomography (CT) or magnetic resonance imaging (MRI) demonstrating either stable or improving metastases 2 or more weeks after completion of radiotherapy.
2. Subject must be asymptomatic and off steroids or on stable dose of steroids for at least 2 weeks (≤ 10 mg daily prednisone or equivalent) prior to first dose.
5. 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 the study treatments.
6. Subject with symptomatic or uncontrolled ulcers (gastric or duodenal), particularly those with a history of and/or risk of perforation and GI tract hemorrhages.
7. Subject with any hemorrhage/bleeding event > NCI CTCAE Grade 2 or haemoptysis > 1 teaspoon within 4 weeks prior to the first dose.
8. Subject has any of the following cardiovascular criteria:
1. Evidence of acute or ongoing cardiac ischemia
2. Current symptomatic pulmonary embolism
3. Unstable angina pectoris or myocardial infarction ≤ 6 months prior to enrollment
4. Heart failure of New York Heart Association Classification III or IV ≤ 6 months prior to enrollment
5. Persistent or clinically meaningful ventricular arrhythmias prior to enrollment
6. Cerebral vascular accident or transient ischemic attack ≤ 6 months prior to enrollment
7. QT corrected based on Fridericia's equation (QTcF) ≥ 450 milliseconds (msec) on Screening ECG, a baseline prolongation of QTcF interval ≥ 450 msec (NCI CTCAE Grade ≥ 2)
8. A history of additional risk factors for Torsades de pointes (TdP) (eg, heart failure, hypokalemia, family history of Long QT Syndrome)
9. Uncontrolled hypertension (blood pressure ≥ 160/95 mm Hg)
9. Subject has known human immunodeficiency virus (HIV) infection.
10. Subject has known chronic active hepatitis B or C virus (HBV, HCV) infection.
1. Subject who is seropositive due to HBV vaccination is eligible.
2. Subject who has no active viral infection and is under adequate prophylaxis against HBV reactivation is eligible.
11. Subject has any other malignancy within 2 years prior to enrollment, with the exception of adequately treated in-situ bladder cancer, in-situ carcinoma of the cervix, uteri, nonmelanomatous skin cancer, ductal in situ breast carcinoma, thyroid cancer, or early stage prostate cancer (all treatment of which should have been completed 6 months prior to enrollment).
12. Subject has medical conditions requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone or equivalent) or other immunosuppressive medications within 14 days of enrollment.
1. A brief (≤ 7 days) course of corticosteroids for prophylaxis (eg, contrast dye allergy) or for treatment of nonautoimmune conditions (eg, delayed-type hypersensitivity reaction caused by contact allergen) is permitted.
2. Adrenal replacement steroid doses ≤ 10 mg daily prednisone or equivalent are permitted in the absence of active autoimmune disease.
3. Topical, ocular, intra-articular, intranasal, and inhalational corticosteroids (with minimal systemic absorption) are permitted.
13. Subject has active autoimmune diseases or history of autoimmune diseases that may relapse. Subjects with the following diseases are allowed to be enrolled after further screening: type I diabetes, hypothyroidism managed with hormone replacement therapy only, skin diseases not requiring systemic treatment (such as vitiligo, psoriasis, or alopecia), or diseases not expected to recur in the absence of external triggering factors.
14. Subject is pregnant or nursing.
15. Subject has a history of persistent skin rash ≥ NCI CTCAE Grade 2 related to prior ICI therapy.
16. Subject has organ transplant history, including allogeneic stem cell transplant.
17. Subject has severe infection requiring a parenteral antibiotic treatment.
18. Subject has interstitial lung disease history.
19. Subject has received a live/attenuated vaccine within 30 days of first dose.

**CONTACTS AND LOCATIONS**

**Contacts**

Contact:

**Locations**

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| United States, Georgia | Augusta University - Georgia Cancer Center | Augusta |
| United States, Indiana | Investigative Clinical Research of Indiana, LLC | Indianapolis |
| United States, New York | Memorial Sloan-Kettering Cancer Center - David H. Koch Center for Cancer Care | New York |
| United States, North Carolina | Novant Health Presbyterian Medical Center | Charlotte |
| United States, North Carolina | Piedmont Hematology Oncology Associates | Winston-Salem |
| United States, Ohio | Gabrail Cancer Center Research | Canton |
| United States, Ohio | University Hospitals Cleveland Medical Center | Cleveland |
| United States, Pennsylvania | University of Pittsburgh Medical Center | Pittsburgh |
| United States, Texas | Brooke Army Medical Center Francis Street Medical Center | Fort Sam Houston |
| United States, Texas | Millennium Oncology | Houston |
| United States, Virginia | Virginia Cancer Specialists, PC | Fairfax |
| France | Hopital Louis Pradel | Lyon Cedex |
| France | Hospital Le Timone | Marseille Cedex 5 |
| France | Hospital Pontchaillou | Rennes |
| France | CHU Nantes Hopital Nord Laennec | Saint-Herblain |
| France | Gustave Roussy | Villejuif CEDEX |
| Italy | Centro di Riferimento Oncologico | Aviano |
| Italy | Istituto Scientifico Romagnolo Per Lo Studio e La Cura Dei Tumori (I.R.S.T.) | Meldola |
| Italy | Fondazione IRCCS Istituto Nazionale dei Tumori | Milan |
| Italy | Policlinico Universitario Campus Biomedico Di Roma | Roma |
| Italy | Azienda Ospedaliera Universitaria Integrata di Verona | Verona |
| Poland | Centrum Terapii Wspolczesnej J.M. Jasnorzewska Spolka Komandytowo-Akcyjna | Lodz |
| Poland | Instytut Centrum Zdrowia Matki Polki | Lodz |
| Poland | Med Polonia Sp. z o.o. NSZOZ | Poznan |
| Poland | Maria Sklodowska-Curie National Research Institute of Oncology | Warsaw |
| Spain | Hospital Universitari Germans Trias i Pujol Can Ruti | Badalona (Barcelona) |
| Spain | Hospital Quiron Barcelona | Barcelona |
| Spain | Hospital Universitari Vall d'Hebron | Barcelona |
| Spain | Insular-Maternal and Child University Hospital Complex | Las Palmas de Gran Canaria |
| Spain | Clinica Universidad de Navarra | Madrid |
| Spain | Hospital Universitario Fundacion Jimenez Diaz | Madrid |
| Spain | Hospital Universitario 12 de Octubre | Madrid |
| Spain | Hospital Puerta de Hierro | Majadahonda, Madrid |
| Spain | Clinica Universidad de Navarra | Pamplona |
| Spain | Hospital Universitari i Politecnic La Fe de Valencia | Valencia |
| United Kingdom | Clatterbridge Centre for Oncology NHS Trust | Bebington, Wirral |
| United Kingdom | The Royal Marsden Hospital | London |
| United Kingdom | The Christie NHS Foundation Trust | Manchester |
| United Kingdom | Royal Marsden Hospital | Sutton-Surrey |

**Sponsors and Collaborators**

Celgene

**Investigator**

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| Study Director : | Ileana Elias, Medical Director | Celgene |

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**MORE INFORMATION**

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| **Responsible Party :** | Celgene |
| **ClinicalTrials.gov Identifier :** | NCT04350463 |
| **Other Study ID Numbers :** | CC-90011-ST-002, U1111-1248-8352, 2019-004194-95 |
| **First Posted :** | April 17, 2020 |
| **Last Update Posted :** | October 2, 2020 |
| **Last Verified :** | September 2020 |
| **Studies a U.S. FDA-regulated Drug Product:** | Yes |
| **Studies a U.S. FDA-regulated Device Product:** | No |
| **Keywords provided by Celgene:** | *CC-90011*<br>*Nivolumab*<br>*Advanced Cancers Small cell lung cancer*<br>*Squamous non-small cell lung cancer*<br>*LSD1 inhibitor* |