CNS Penetration, PK and PD of Preoperative CC-90010 in Progressive/Recurrent Diffuse Astrocytoma, Anaplastic Astrocytoma and Glioblastoma

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT04047303	RECRUITING	AUGUST 6, 2019	JULY 24, 2020

STUDY DESCRIPTION

Brief Summary

CC-90010-GBM-001 is a multi-center, open-label study to assess the pharmacokinetics (PK), pharmacodynamics (PD) and CNS penetration of CC-90010 following short-term interval therapy (4 daily doses) prior to surgery, in subjects with progressive or recurrent WHO Grade II Diffuse Astrocytoma, Grade III Anaplastic Astrocytoma and recurrent Glioblastoma who have failed radiation and chemotherapy, and who are candidates for surgical tumor resection as part of their salvage regimen (planned salvage resection).

Condition or Disease: Astrocytoma
Glioblastoma

Intervention/treatment: Drug: CC-90010

Phase: Phase 1/Phase 2

DETAILED DESCRIPTION

N/A

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 10 participants

Intervention Model : Single Group Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: A Phase 1, Open-label Study to Assess the Pharmacokinetics, Pharmacodynamics and Central Nervous System (CNS) Penetration of CC-90010 in Preoperative Subjects With Progressive or Recurrent Who Grade II Diffuse Astrocytoma, Grade III Anaplastic Astrocytoma and Recurrent Glioblastoma Scheduled for Resection

Actual Study Start Date: January 2020

Estimated Primary Completion Date: March 2021

Estimated Study Completion Date: August 2021

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: Administration of CC-90010 During the preoperative period, all subjects will be given a course of orally administrated CC-90010 at 30 mg once daily for 4 consecutive days on Cycle 1 Day 1 to Day 4. The last CC-90010 dose (Day 4) will be administrated 6-24 hours prior to brain tumor resection. Following recovery from surgery and a minimum of 4 weeks from the first CC-90010 dose (Cycle 1 Day 1), subjects who are fit to continue study treatment my restart CC-90010 on Day 1 of Cycle 2 at 45 mg given orally once daily for 4 consecutive days followed by 24 consecutive days off (4 days on/24 days off), in each 28 day cycle.	Drug: CC-90010 CC-90010

OUTCOME MEASURES

Primary Outcome Measures: 1. Intratumoral concentration of CC-90010 in tumor tissue collected intraoperatively [Time Frame: Up to 4 days following C1D1]
Intratumoral concentration of CC-90010 will be summarized using descriptive statistics
2. Pharmacokinetics - AUC24 [Time Frame: At the end of Cycle 1 (each cycle is 28 days)]
Area under the plasma concentration time-curve
3. Pharmacokinetics - AUClast [Time Frame: At the end of Cycle 1 (each cycle is 28 days)]
Area under the plasma concentration time-curve
4. Pharmacokinetics - Cmax [Time Frame: At the end of Cycle 1 (each cycle is 28 days)]
Maximum observed plasma concentration
5. Pharmacokinetics - Tmax [Time Frame: At the end of Cycle 1 (each cycle is 28 days)]
Time to maximum plasma concentration
6. Pharmacokinetics - t1/2 [Time Frame: At the end of Cycle 1 (each cycle is 28 days)]
Terminal half-life
7. Pharmacokinetics - CL/F [Time Frame: At the end of Cycle 1 (each cycle is 28 days)]
Apparent clearance
8. Pharmacokinetics - V2/F [Time Frame: At the end of Cycle 1 (each cycle is 28 days)]
Apparent volume of distribution

Secondary Outcome Measures:	1. Adverse Events (AEs) [Time Frame: From enrollment until at least 28 days after completion of study treatment] Number of participants with adverse event

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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. Men and women ≥ 18 years of age,) with recurrent or progressive WHO Grade II Diffuse Astrocytoma, Grade III Anaplastic Astrocytoma or recurrent WHO Grade IV Glioblastoma .
2. Subjects must have previously completed standard or a hypofractionated course of radiation therapy and have been exposed to procarbazine, lomustine and vincristine (for Grade II Astrocytoma), including those who have progressed on (or not been able to tolerate due to medical comorbidities or unacceptable toxicity) standard anticancer therapy, with radiation completed > 12 weeks prior to the first CC-90010 dose (Day 1).
3. Subject must be in first or second recurrence.
4. Subject must have archival tumor tissue suitable for genetic testing and must give permission to access and test the tissue.
5. Subject is considered an appropriate candidate for surgical resection of the recurrent tumor tissue (salvage resection).
6. Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 to 1.
7. Subject must meet laboratory values at screening:
- Absolute neutrophil count (ANC) ≥ 1.5 x 109/L without growth factor support for 7 days (14 days if subject received pegfilgrastim).
- Hemoglobin (Hgb) ≥10 g/dL
- Platelet count (plt) ≥150 x 109/L
- Serum potassium concentration within normal range, or correctable with supplements
- Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 3.0 x Upper Limit of Normal (ULN).
- Serum total bilirubin ≤ 1.5 x ULN.
- Serum creatinine ≤ 1.5 x ULN or measured glomerular filtration rate (GFR) ≥ 50 mL/min/1.73 m2 using an exogenous filtration marker such as iohexol, inulin, 51Cr EDTA or 1 iothalamate, or creatinine clearance of ≥ 50 mL/min using Cockroft-Gault equation.
- Serum albumin > 3.5 g/dL
- PT (or INR) and APTT within normal range
8. Females and males must agree to contraceptive methods and avoid conceiving throughout study and up to 3 months (females) and 106 days (males) following last dose of CC-90010.
Exclusion Criteria:
The presence of any of the following will exclude a subject from enrollment:
1. Subject has received anti-cancer therapy (either approved or investigational) within ≤ 4 weeks (6 weeks for nitrosoureas) or 5 half-lives, whichever is shorter, prior to starting CC-90010. If subject received prior immunotherapy (immune checkpoint inhibitor, vaccine, etc.), a 2 week wash-out is required. For a subject treated with the Optune-TTF device, a 2 day period without use is required.
2. Toxicities resulting from prior chemotherapy, surgery, or radiotherapy must have resolved to ≤ NCI CTCAE (version 5.0) Grade 1 prior to starting CC-90010 treatment (with the exception of Grade 3 alopecia).
3. Subject has undergone major surgery ≤ 4 weeks or minor surgery ≤ 2 weeks prior to starting CC-90010 or subject who has not recovered from surgery.
4. 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-90010.
5. Subject with symptomatic or uncontrolled ulcers (gastric or duodenal), particularly those with a history of and/or risk of perforation and GI tract hemorrhages.
6. Evidence of CNS hemorrhage on baseline MRI or CT scan (except for post-surgical, asymptomatic Grade 1 hemorrhage that has been stable for at least 4 weeks).
7. Subject who requires increasing doses of corticosteroids to treat symptomatic cerebral edema within 7 days of study therapy.
8. Known symptomatic acute or chronic pancreatitis.
9. Impaired cardiac function or clinically significant cardiac diseases, including any of the following:
- LVEF < 45% as determined by multiple gated acquisition scan (MUGA) or echocardiogram (ECHO). - Complete left bundle branch or bifascicular block. - Congenital long QT syndrome. - Persistent or clinically meaningful ventricular arrhythmias or atrial fibrillation. - QTcF ≥ 480 msec on Screening ECG (mean of triplicate recordings); a marked baseline prolongation of QT/QTc interval, using Fridericia´s QT correction formula. - History of additional risk factors for Torsade de Pointes (TdP) (e.g. heart failure, hypokalemia, family history of Long QT syndrome. - Use of concomitant medications that prolong the QT/QTc interval. - Unstable angina pectoris or myocardial infarction ≤ 6 months prior to starting CC-90010. - Other clinically significant heart disease such as congestive heart failure requiring treatment or uncontrolled hypertension (blood pressure ≥ 160/95 mm Hg). 10. Pregnant or nursing females. 11. Known HIV infection. 12. Known chronic active hepatitis B or C virus (HBV, HCV) infection. 13. Subject with a requirement for ongoing treatment with therapeutic dosing of anticoagulants or for ongoing prophylactic anticoagulation. Low dose low molecular weight heparin for catheter maintenance is allowed. 14. History of concurrent second cancers requiring active, ongoing systemic treatment. 15. Evidence of history of bleeding diathesis. 16. Subject 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. 17. Subject with poor bone marrow reserve as assessed by Investigator such as in the following condition: - Requiring regular hematopoietic support

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CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

United States, Florida	Mayo Clinic - Jacksonville	Jacksonville
United States, Florida	Moffit Cancer Center	Tampa
United States, Massachusetts	Dana Farber Cancer Institute	Boston

Spain	Hospital Universitario Fundacion Jimenez Diaz	Madrid
Spain	Hospital Universitario 12 de Octubre	Madrid

Sponsors and Collaborators

Celgene

Investigator

Study Director : Zariana Nikolova, MD, PhD Celgene Corporation

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MORE INFORMATION

Responsible Party :	Celgene
ClinicalTrials.gov Identifier :	NCT04047303
Other Study ID Numbers :	CC-90010-GBM-001, U1111-1235-8082, 2019-000241-12
First Posted :	August 6, 2019
Last Update Posted :	July 24, 2020
Last Verified :	July 2020
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:	*Diffuse Astrocytoma* *Anaplastic Astrocytoma* *CC-90010 CNS* *2nd line or relapsed* *Glioblastoma*
Additional relevant MeSH terms :	*Glioblastoma* *Astrocytoma*