Testing the Addition of Anti-cancer Drug, ZEN003694, to the Usual Chemotherapy Treatment, Cetuximab Plus Encorafenib, for Colorectal Cancer

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Patients must have histologically confirmed and radiographically measurable metastatic colorectal adenocarcinoma with known BRAF V600E mutation, confirmed in a Clinical Laboratory Improvement Amendments (CLIA) certified laboratory with at least one tumor measurable as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, and for which standard curative or palliative measures do not exist or are no longer effective * Age ≥ 18 years. Because no dosing or adverse event data are currently available on the use of ZEN003694 in combination with cetuximab and encorafenib in patients \< 18 years of age, children are excluded from this study * Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 (Karnofsky ≥ 60%) * Absolute neutrophil count ≥ 1,500/mcL * Platelets ≥ 100,000/mcL * Hemoglobin (Hb) ≥ 9 mg/dl * Total bilirubin ≤ 1.5 mg/dl (excluding Gilbert's disease) * Aspartate aminotransferase (AST) (serum glutamic-oxaloacetic transaminase \[SGOT\])/alanine aminotransferase (ALT) (serum glutamate pyruvate transaminase \[SGPT\]) ≤ 3 x institutional upper limit of normal (ULN) * Creatinine clearance (CrCL) glomerular filtration rate (GFR) ≥ 50 mL/min/1.73 m\^2 * Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial * For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated * Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load * Patients with treated brain metastases are eligible if follow-up brain imaging after central nervous system (CNS)-directed therapy shows no evidence of progression * Patients with new or progressive brain metastases (active brain metastases) or leptomeningeal disease are eligible if the treating physician determines that immediate CNS specific treatment is not required and is unlikely to be required during the first cycle of therapy * Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial * Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification. Patients should be New York Heart Association Functional Classification of class II or better * Patients must have progressed after at least 1 prior systemic treatment for incurable advanced or metastatic disease * Patients must have received prior treatment with the combination of encorafenib and cetuximab. They must have tolerated the combination at doses planned for the study * The effects of ZEN003694 on the developing human fetus are unknown. For this reason and because BRD and BET inhibitor agents as well as other therapeutic agents used in this trial are known to be teratogenic, women of child-bearing potential and men must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to study entry, for the duration of study participation, and for at least 4 months following the last dose of study drug. Women must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of human chorionic gonadotropin \[HCG\]) within 72 hours prior to the start of investigational product. Should a woman become pregnant or suspect she is pregnant while she or her partner is participating in this study, she should inform her treating physician immediately * Ability to understand and the willingness to sign a written informed consent document. Legally authorized representatives may sign and give informed consent on behalf of study participants

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Exclusion Criteria:

* Patients who have not recovered from adverse events due to prior anti-cancer therapy (i.e., have residual toxicities \> grade 1) with the exception of alopecia * Patients who are receiving any other investigational agents * History of allergic reactions attributed to compounds of similar chemical or biologic composition to ZEN003694 or other agents used in study * Patients with uncontrolled intercurrent illness including, but not limited to, active bleeding diatheses, poorly controlled infection/disorders, or nonmalignant medical illnesses that are uncontrolled or whose control may be jeopardized by the treatment with the study therapy * Patients receiving any medications or substances that are strong inhibitors or inducers of CYP3A4 or substrates of CYP1A2 with narrow therapeutic windows are ineligible. Strong inhibitors or inducers of CYP3A4 must be discontinued at least 7 days prior to the first dose of ZEN003694. As proton pump inhibitors (PPIs), H2 receptor antagonists, and antacids may alter the pharmacokinetics of ZEN003694 by reducing ZEN003694 exposure, patients receiving proton pump inhibitors are ineligible. If H2 blockers or other acid reducing agents are used concomitantly with ZEN003694, a staggered dosing schedule should be used, either dose ZEN003694 2 hours before the H2 blocker or 10-12 hours after an H2 blocker. Because the lists of these agents are constantly changing, it is important to regularly consult a frequently-updated medical reference. As part of the enrollment/informed consent procedures, the patient will be counseled on the risk of interactions with other agents, and what to do if new medications need to be prescribed or if the patient is considering a new over-the-counter medicine or herbal product * Pregnant women are excluded from this study because ZEN003694 is BRD and BET inhibitor agent with the potential for teratogenic or abortifacient effects. Because there is an unknown but potential risk for adverse events in nursing infants secondary to treatment of the mother with ZEN003694, breastfeeding should be discontinued if the mother is treated with ZEN003694. These potential risks may also apply to other agents used in this study

Conditions & Interventions

Interventions:

DRUG: BET Bromodomain Inhibitor ZEN-3694, PROCEDURE: Biopsy Procedure, PROCEDURE: Biospecimen Collection, BIOLOGICAL: Cetuximab, PROCEDURE: Computed Tomography, PROCEDURE: Echocardiography Test, DRUG: Encorafenib, PROCEDURE: Magnetic Resonance Imaging, PROCEDURE: Multigated Acquisition Scan

Conditions:

Metastatic Colorectal Adenocarcinoma, Recurrent Colorectal Adenocarcinoma, Refractory Colorectal Adenocarcinoma, Stage IV Colorectal Cancer AJCC v8

More Information

Contact(s): ctrrecruit@vcu.edu

Principal Investigator:

Phase: PHASE1

IRB

Number:

System ID: NCT06102902
