Neratinib + Valproate in Advanced Solid Tumors, w/Expansion Cohort in Ras-Mutated Ca

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Phase 1

•Dose Escalation Phase: Advanced solid tumor that has progressed during or after treatment with approved therapies or for which there is no standard effective therapy available * Phase 2

•Dose Expansion Phase: One of the following advanced solid tumors that is RAS-mutated and has progressed during or after treatment with at least one approved therapy or for which there is no standard effective therapy available: : * Colon Cancer with a RAS mutation * Pancreatic Cancer with a RAS mutation * Other Solid Tumor with RAS Mutation * Ocular melanoma, which includes melanoma that develops in the sclera, retina, uvea (iris, choroid layer, and ciliary layer), or conjunctiva or other cancers with a GNAQ or GNA11 mutation * Measurable disease by RECIST v1.1 * Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 * Adequate bone marrow function * Absolute neutrophil count (ANC) ≥ 1500/mm3 * Platelets ≥ 100,000/mm3 * Hemoglobin \> 9 g/dL (untransfused) * Adequate renal function * Creatinine ≤ 1.5 x upper limit of normal (ULN) for the laboratory or calculated or actual creatinine clearance ≥ 60 mL/min * Adequate hepatic function * Total bilirubin ≤ 1.5 x ULN for the laboratory Exception: If a patient has documented Gilbert's syndrome and a total bilirubin is \> 1.5 x ULN for the laboratory, the total bilirubin requirement may be waived provided the direct bilirubin is within normal limits (WNL) for the laboratory. * Aspartate aminotransferase (AST) ≤ 3.0 x ULN for the laboratory * Alanine aminotransferase (ALT) ≤ 3.0 x ULN for the laboratory * Note: For the expansion cohorts, in patients with documented liver metastasis, the AST and ALT requirements will be ≤ 5 x ULN for the laboratory * Non-hematologic toxicities from previous cancer therapies resolved to ≤ grade 1 except chronic residual toxicities that in the opinion of the investigator are not clinically relevant given the known safety/toxicity profiles of neratinib and sodium valproate (eg, alopecia, changes in pigmentation, stable endocrinopathies, neuropathy, skin toxicities) * International normalized ratio (INR) is ≤ 1.5 and activated partial thromboplastin time (aPTT) ≤ 1.5 x ULN for the laboratory * A woman of childbearing potential (WCBP), defined as a woman who is \< 60 years of age and has not had a hysterectomy, must have a documented negative serum pregnancy test within 7 days prior to initiating study treatment * WCBP and a male patient with a partner who is a WCBP must agree to use a medically accepted method for preventing pregnancy for the duration of study treatment and for 2 months following completion of study treatment * Ability to understanc and willingness to sign a written informed consent document

---

Exclusion Criteria:

Current or prior known meningeal metastases Known brain metastases that are symptomatic or untreated Note: Patients with known brain metastases who are asymptomatic and have had post-treatment imaging that indicates stable brain disease are eligible. Note that brain imaging in patients with known brain metastases is required within 8 weeks prior to initiation of study therapy. * Any investigational agent within 4 weeks prior to initiating study treatment * Previous therapy with neratinib * Active uncontrolled diarrhea leading to dehydration or electrolyte disturbances not easily controlled with oral repletion * Inability to swallow medication * Known or suspected malabsorption condition or obstruction. Note: Use of pancreatic enzyme supplements is allowed to control malabsorption * Inability to shift medications as follows: Antacids (eg, calcium carbonate): dose at least 3 hours after dosing with neratinib. H2 receptor antagonists: dose must be taken at least 2 hours after or 10 hours before dosing with neratinib * Resting systolic blood pressure (BP) \< 100 mmHg * Active or clinically significant cardiac disease including any of the following: * Unstable angina (eg, anginal symptoms at rest) or onset of angina within 3 months prior to initiating study treatment * Myocardial infarction diagnosed within 6 months prior to initiating study treatment * Cardiac arrhythmias requiring anti-arrhythmic therapy other than beta blockers * New York Heart Association (NYHA) class III or IV congestive heart failure * Seizure disorder requiring an enzyme inducing antiepileptic medication (EIAED) * Serious (ie, ≥ grade 3) uncontrolled infection * Chronic or active hepatitis B or C infection with elevated transaminase levels * Pleural effusion or ascites that causes respiratory compromise (ie, ≥ grade 2 dyspnea) * Known mitochondrial disorder caused by mutations in mitochondrial DNA polymerase gamma (γ) * Known urea cycle disorders * Planned ongoing treatment with other drugs thought to potentially have adverse interactions with either of the medications included in the study treatment: * Cosyntropin * Proton pump inhibitors (PPIs) * High-risk P-glycoprotein (P-gp) substrates (eg, digoxin, dabigatran, fexofenadine). Other anticoagulants are not considered high-risk P-gp substrates * Strong or moderate CYP3A4 inhibitors and/or Strong or moderate CYP3A4 inducers. Examples of clinical inhibitors and clinical inducers for P450-mediated metabolism and classification of strong, moderate, and weak interactions are available through the FDA website, Tables 3-2 and 3-3: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionsLabeling/ucm093664.htm Note: If such medications have been used, patients must have discontinued these agents ≥ 2 weeks prior to initiating study treatment * Pregnancy or breastfeeding * Medical, psychological, or social condition that, in the opinion of the investigator, may increase the patient's risk or limit the patient's adherence with study requirements

Conditions & Interventions

Interventions:
DRUG: Neratinib, DRUG: Divalproex Sodium
Conditions:
Solid Tumor, Adult
Keywords:
Colon Cancer, Pancreatic Cancer, Other solid tumor, Advanced solid tumor, Tumor progression

More Information

Contact(s): Massey IIT Research Operations - masseysiit@vcu.edu
Principal Investigator: Poklepovic, Andrew, S
Phase: PHASE1
IRB Number: HM20015913
System ID: NCT03919292

Thank you for choosing StudyFinder. Please visit http://studyfinder.cctr.vcu.edu to find a Study which is right for you and contact ctrrecruit@vcu.edu if you have questions or need assistance.