

Using Nivolumab Alone or With Cabozantinib to Prevent Mucosal Melanoma Return After Surgery

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* STEP 0 INCLUSION CRITERIA * Histologically proven mucosal melanoma by local pathology * Central PD-L1 tumor tissue submission * STEP 1 INCLUSION CRITERIA * Receipt of the central PD-L1 testing results available * Report is required for randomization of resection R0 or R1 patients * Testing must be started in Step 0 but results can be reported after registration for resection R2 patients * Disease status-Resected R0 or R1 disease patients. Patients eligible for randomization have resected R0 or R1 disease (with negative margins or positive microscopic margins) that must meet one of the following 4 criteria as defined below: * Regional lymph node (LN) involvement; OR * In-transit metastases/satellite primary disease; OR * Single localized, primary disease meeting one of the following site-specific requirements: * Head/neck

•Sinonasal (including nasopharynx): any primary lesion; Nasal or oral cavity; pT4a or above, given slightly improved OS * NOTE: Conjunctival: does not meet the qualification for eligibility * Anorectal

•any primary lesion * Vaginal/cervical

•any primary, as they have 5 year OS rates of 5-25% * Urinary tract

•any primary urethral or bladder tumor * Penile * Vulvar- American Joint Committee on Cancer (AJCC) cutaneous stage IIB or higher * Esophageal/gallbladder

•any primary * Locoregionally recurrent following prior resection, meeting at least one of the above criteria * In addition, patients must have undergone cross-sectional imaging of the brain, chest, abdomen and pelvis with no evidence of distant metastatic disease * Disease status-Non-resected R2 or metastatic disease patients * Non-resected R2 or metastatic disease that is assessable and measurable radiographically or by physical examination * Prior Treatment: * No prior systemic checkpoint inhibitor therapy of mucosal melanoma, including in the adjuvant setting, is allowed. Prior adjuvant chemotherapy or interferon is allowed. * No other active, concurrent malignancy that requires ongoing systemic treatment or interferes with radiographic assessment of melanoma response as determined by the investigator. Exceptions may allow for adjuvant no evidence of disease (NED) cancers undergoing hormone based therapy may be eligible pending the other eligibility criteria are met and the principal investigator (PI) affirms the hormonal agent would not change the melanoma response. * Any radiation must have completed 28 days prior to randomization and the patient must have adequately recovered from its effects. * For resectable patients only: Surgery must have completed 28 days prior to randomization. * For resectable patients only: Surgery must have completed no more than 84 days prior to randomization. * Not pregnant and not nursing, because this study has an agent that has known genotoxic, mutagenic and teratogenic effects. Therefore, for women of childbearing potential only, a negative pregnancy test done =< 7 days prior to registration is required * Age >= 18 years * Eastern Cooperative Oncology Group (ECOG) performance status 0-2 * Absolute neutrophil count (ANC) >= 1,500/mm^3 * Platelet count >= 100,000/mm^3 * Creatinine =< 1.5 x upper limit of normal (ULN) OR creatinine clearance (CrCl) >= 50mL/min/1.73 m^2 for patients with creatinine levels above institutional normal * Albumin >= 2.8 g/dL * Total bilirubin =< 1.5 x upper limit of normal (ULN) * Aspartate aminotransferase (AST)/alanine aminotransferase (ALT) =< 2.5 x upper limit of normal (ULN) * No cardiovascular disease, including: * No history of acute coronary syndromes (including myocardial infarction and unstable angina), coronary artery bypass graft (CABG) coronary angioplasty, or stenting within 6 months prior to study entry. * No history of current class II or higher congestive heart failure as defined by the New York Heart Association (NYHA) functional classification system. * No refractory hypertension defined as a blood pressure of systolic > 140 mmHg and/or diastolic > 90 mmHg despite adequate attempts at anti-hypertensive therapy. * No history of myocarditis. * No history of syncope of cardiovascular etiology, uncontrolled cardiac arrhythmia, history of Mobitz II second degree or third degree heart block without a permanent pacemaker in Association (NYHA) class II to IV heart failure, or stroke/transient ischemic attack (TIA) within the past 3 months. * No corrected QT interval by Fridericia's formula (QTcF) > 500 msec. Note: if initial QTcF is found to be > 500 ms, two additional electrocardiograms (EKGs) separated by at least 3 minutes should be performed. If the average of these three consecutive results for QTcF is =< 500 ms, the subject meets eligibility in this regard. * No underlying hematologic issues, including: * Congenital bleeding diathesis * Gastrointestinal (GI) bleeding requiring intervention within the past 6 months, unless directly related to mucosal melanoma * Active hemoptysis within 42 days prior to study enrollment. * Active tumor lesions with cavitations or tumor lesions which invade, encase, or abut major blood vessels. The anatomic location and characteristics of primary tumors or metastases as well as the medical history should be carefully reviewed in the selection of subjects for treatment with cabozantinib/placebo. * Pulmonary emboli or deep vein thromboses (DVT) that require an active anticoagulation regimen. * No known or suspected history of cytopenia (low white blood cell [WBC], hemoglobin or platelet count) of greater than 3 months duration with an unknown cause, myelodysplastic syndrome, or hematologic malignancies. * No clinical, laboratory or radiographic evidence of an active bacterial, fungal, or viral infection requiring treatment at the time of pre-registration (e.g., active symptoms of COVID-19 infection or a post-infectious symptomatic autoimmune syndrome, serious bacterial infections requiring antibiotics). * No known or suspected gastrointestinal disorder affecting absorption of oral medications. * Comorbid conditions: * No active autoimmune disease or any condition requiring systemic treatment with either corticosteroids (> 10 mg daily of prednisone equivalents) or other immunosuppressive medications within 14 days of study drug administration. Inhaled or topical steroids and adrenal replacement doses > 10 mg daily prednisone equivalents are permitted in the absence of active autoimmune disease. * No history of autoimmune motor neuropathy (e.g., Guillain-Barre syndrome, myasthenia gravis) or non-infectious pneumonitis. * No history of severe allergic reactions to an unknown allergen or any components of the study drugs or its excipients. * No history of gastrointestinal perforation or abdominal fistula. * No clinically suspected central nervous system (CNS) (leptomeningeal or parenchymal) metastases. Patients with a history of CNS metastasis(s) will be allowed as long as * The metastatic site(s) were adequately treated as demonstrated by clinical and radiographic improvement, AND * The patient has recovered from the intervention (no residual adverse events > Common Terminology Criteria for Adverse Events [CTCAE] grade 1), AND * The patient has remained without occurrence of new or worsening CNS symptoms for a period of 28 days prior to enrollment. * No history of seizure or any condition that may increase the patient's seizure risk (e.g., prior cortical stroke, significant brain trauma) within 2 years. * No clinically active or chronic liver disease resulting in moderate/severe hepatic impairment (Child-Pugh class B or C), ascites, coagulopathy or bleeding due to liver dysfunction. * No untreated spinal cord compression or evidence of spinal metastases with a risk of impending fracture or spinal cord compression. Spinal metastases must have completed planned radiation or surgical therapy prior to registration. * Concomitant medications: * Chronic concomitant treatment with strong inhibitors of CYP3A4 is not allowed on this study. Patients on strong CYP3A4 inhibitors must discontinue the drug for 5 days prior to the start of study treatment. * Chronic concomitant treatment with strong CYP3A4 inducers is not allowed. Patients must discontinue the drug 5 days prior to the start of study treatment.

Conditions & Interventions

Interventions:

PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Scan, DRUG: Cabozantinib S-malate, PROCEDURE: Computed Tomography, PROCEDURE: Echocardiography Test, PROCEDURE: Magnetic Resonance Imaging, BIOLOGICAL: Nivolumab, DRUG: Placebo Administration, PROCEDURE: Positron Emission Tomography

Conditions:

Anal Melanoma, Bladder Melanoma, Cervical Melanoma, Esophageal Melanoma, Gallbladder Melanoma, Head and Neck Mucosal Melanoma, Mucosal Melanoma

Anal melanoma, Bladder melanoma, Cervical melanoma, Esophageal melanoma, Gallbladder melanoma, Head and Neck mucosal melanoma, Mucosal melanoma, Nasopharyngeal Mucosal Melanoma, Oral Cavity Mucosal Melanoma, Penile Mucosal Melanoma, Rectal Melanoma, Recurrent Mucosal Melanoma, Sinonasal Mucosal Melanoma, Urethral Melanoma, Urinary System Mucosal Melanoma, Vaginal Melanoma, Vulvar Melanoma

More Information

Contact(s): ctrrecruit@vcu.edu

Principal Investigator:

Phase: PHASE2

IRB

Number:

System ID: NCT05111574

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