Testing the Addition of an Anti-cancer Drug, ASTX727 (Cedazuridine, Decitabine), to Chemotherapy (Paclitaxel) and Immunotherapy (Pembrolizumab) for Metastatic Triple-Negative Breast 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 triple-negative breast cancer (TNBC) (estrogen receptor \[ER\] and progesterone receptor \[PR\] =\< 10%, human epidermal growth factor receptor-2 \[HER2\]-negative per American Society of Clinical Oncology \[ASCO\]/College of American Pathologists \[CAP\] guidelines) that is metastatic or unresectable * Age \>= 18 years. Because no dosing or adverse event data are currently available on the use of ASTX727 in combination with pembrolizumab (MK-3475) and paclitaxel in patients \< 18 years of age, children are excluded from this study * Eastern Cooperative Oncology Group (ECOG) performance status =\< 2 (or Karnofsky \>= 60%) * Absolute neutrophil count (ANC) \>= 1500/mm\^3 (within 14 days prior to registration) * Platelets \>= 100,000/mm\^3 (within 14 days prior to registration) * Hemoglobin \>= 9 g/dL or \>= 5.6 mmol/L (within 14 days prior to registration) * Criteria must be met without packed red blood cell (pRBC) transfusion within the prior 14 days of registration. Participants can be on stable dose of erythropoietin (90 days or more prior to registration) * Creatinine clearance (CrCl) \>= 30 mL/min (within 14 days prior to registration) * Glomerular filtration rate (GFR) can also be used in place of CrCl * Total bilirubin =\< 1.5 x upper limit of normal (ULN) OR direct bilirubin =\< ULN for patients with total bilirubin levels \> 1.5 × ULN (within 14 days prior to registration) * Aspartate aminotransferase (AST) (serum glutamic-oxaloacetic transaminase \[SGOT\]) and alanine aminotransferase (ALT) (serum glutamic-pyruvic transaminase \[SGPT\]) =\< 3 x institutional ULN (within 14 days prior to registration) * 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 there is evidence of measurable extracranial disease, and if follow-up brain imaging 4 weeks after central nervous system (CNS)-direct therapy shows no evidence of progression. Patients with carcinomatous meningitis are not eligible. * Patients with a prior malignancy whose natural history does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial. Concurrent use of other antineoplastic treatments is not allowed. * Patients should be New York Heart Association Functional Classification of class II or better. * Patients who have received live attenuated vaccines within the 30 days prior to registration are not eligible. Seasonal flu vaccines that do not contain live virus, and coronavirus disease 2019 (COVID-19) vaccinations and boosters are permitted. * Patients with prior history of peripheral neuropathy are allowed if it has recovered to grade 1 or less. * Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of registration are eligible for this trial. * Patients who have received 0-3 prior lines of chemotherapy in the metastatic setting. Patients who have received prior PD-1/PD-L1 monoclonal antibodies in any disease setting are eligible. * For enrollment to Dose Finding Cohort: Availability and willingness to provide archival tumor tissue as required per protocol. * For enrollment to Dose Expansion Cohort: (i) Willingness to provide baseline and 3-week tumor tissue biopsy specimens. (ii) Patients must have a measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1. * The effects of ASTX727 and pembrolizumab (MK-3475) on the developing human fetus are unknown. For this reason and because these 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 180 days after the last dose of study treatment. 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. Pregnant women are excluded from this study because pembrolizumab (MK-3475) is an anti PD-1 monoclonal antibody agent, ASTX727 is a hypomethylating agent, and paclitaxel is a class D 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 pembrolizumab (MK-3475), breastfeeding should be discontinued if the mother is treated with pembrolizumab (MK-3475). These potential risks may also apply to other agents used in this study. Men treated or enrolled on this protocol must also agree to use adequate contraception prior to the study, for the duration of study participation, and 180 days after completion of study treatment. * Ability to understand and the willingness to sign a written informed consent document (or have legally acceptable representative sign, if applicable). * Patients who have recovered from adverse events due to prior anti-cancer therapy (i.e., have residual toxicities \> grade 1) with the exception of alopecia. * Note: If patients received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting therapy. * Has not received transfusion of blood products (including platelets or red blood cells) or administration of colony stimulating factors (including granulocyte colony-stimulating factor \[G-CSF\], granulocyte macrophage colony-stimulating factor \[GM-CSF\], or recombinant erythropoietin) within 4 weeks prior to registration.

Exclusion Criteria:

* Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within the 7 days prior to registration. * Has a known additional malignancy that is progressing or requires active treatment. * Has an active autoimmune disease that has required systemic treatment within 2 years prior to registration (i.e., with use of disease modifying agents, corticosteroids, or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment. Current treatment with systemic steroids up to 10 mg of prednisone daily or equivalent is allowed. * Patients with uncontrolled intercurrent illness (including but not limited to interstitial lung disease or active, non-infectious pneumonitis) or a history of (non-infectious) pneumonitis that required steroids. * History of grade 3-4 immediate hypersensitivity reaction to paclitaxel or other drugs formulated in polyoxyl 35 castor oil. * Patients who are receiving any other investigational agents. * History of allergic reactions attributed to compounds of similar chemical or biologic composition to ASTX727, pembrolizumab (MK-3475), and/or paclitaxel. * Has a known history of active tuberculosis (TB). * Gastrointestinal disorder that may impact absorption of oral medications. * History of solid organ or bone marrow transplantation.

Conditions & Interventions

Interventions:

PROCEDURE: Biopsy Procedure, PROCEDURE: Biospecimen Collection, PROCEDURE: Computed Tomography, DRUG: Decitabine and Cedazuridine, PROCEDURE: Magnetic Resonance Imaging, DRUG: Paclitaxel, BIOLOGICAL: Pembrolizumab

Conditions:

Anatomic Stage III Breast Cancer AJCC v8, Anatomic Stage IV Breast Cancer AJCC v8, Metastatic Triple-Negative Breast Carcinoma, Unresectable Triple-Negative Breast Carcinoma

More Information

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IRB
Number:
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