Testing the Combination of the Anti-cancer Drugs ZEN003694 (ZEN-3694) and Talazoparib in Patients With Advanced Solid Tumors, The ComBET Trial

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 malignancy that is metastatic or unresectable and for which standard curative or palliative measures do not exist or are no longer effective * Patients must have a tumor lesion that can be biopsied with 'low' or 'minimal' risk and at least one measurable disease site, as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version (v) 1.1 * Note: Tumor lesions that are situated in a previously irradiated area may or may not be considered measurable * Patients in cohorts 1, 2, and 4 should have at least one relevant mutation. Patients enrolled in cohorts 1-3 do not require that PARP inhibitor (i) be the immediate prior therapy to be eligible for the trial. Patients should sign a screening consent that will allow the review of local next generation sequencing (NGS) or equivalent Clinical Laboratory Improvement Act (CLIA)-certified assay results by MD Anderson's Precision Oncology Decision Support (PODS) team to ensure that the mutations are actionable. No variants of uncertain significance (VUS) will be allowed * Patients in Cohort 1 must have (i) a germline or somatic mutation in BRCA1 or BRCA2; and (ii) must have received prior PARPi monotherapy or PARPi combination-therapy * Patients in Cohort 2 must have: (i) a germline or somatic mutation in any of the following deoxyribonucleic acid (DNA) damage response (DDR) genes: BARD1; FANCA; BRIP1; PALB2; RAD51; RAD51C; RAD51D, with no evidence of mutations in BRCA1 or BRCA2; and (ii) must have received prior PARPi monotherapy or PARPi combination therapy * Patients in Cohort 3 must be (i) patients who have had PR/CR on prior PARPi monotherapy or PARPi combination treatment; and (ii) patients with no evidence of BRCA1 or BRCA2 mutations or any of the relevant DDR aberrations listed in cohort 2. Patients with ovarian cancer should not have progressed on platinum-therapy within six months of therapy * Patients in Cohort 4 must have KRAS mutated advanced solid tumors. Prior treatments with KRAS inhibitors are permitted. Patients with KRAS G12C mutations must have already had KRAS G12C targeted therapy (e.g., sotorasib) previously * Patients must have received at least one line of systemic therapy in the advanced/metastatic setting. Subjects with diseases without known effective options, and subjects who have declined standard of care therapy prior to study introduction, are also eligible. Patients with ovarian cancer in cohort 3 should not have progressed on platinum within six months of therapy * Age \>= 18 years * Because no dosing or adverse event data are currently available on the use of ZEN003694 (ZEN-3694) in combination with talazoparib in patients \< 18 years of age, children are excluded from this study * Patients must be greater than 4 weeks (6 weeks for nitrosoureas or mitomycin C) beyond treatment with any chemotherapy or other investigational therapy including hormonal, biological, or targeted agents; or at least 5 half-lives from hormonal, biological, or targeted agents, whichever is shorter at the time of treatment initiation. Patients must have recovered from adverse events due to prior anti-cancer therapy (i.e., have residual toxicities =\< grade 1) with the exception of alopecia or anorexia * Eastern Cooperative Oncology Group (ECOG) performance status =\< 2 (Karnofsky \>= 60%) * Absolute neutrophil count \>= 1,500/mcL * Platelets \>= 150,000/mcL * Hemoglobin \>= 10.0 g/dL (no blood transfusions in the preceding 28 days) * Total bilirubin 1.5 x =\< institutional upper limit of normal (ULN) OR direct bilirubin = ULN for subjects with total bilirubin levels \> 1.5 x ULN * Aspartate aminotransferase (AST) (serum glutamic-oxaloacetic transaminase \[SGOT\])/alanine aminotransferase (ALT) (serum glutamate pyruvate transaminase \[SGPT\]) =\< 2.5 x institutional ULN * Creatinine 1.5 x institutional ULN OR glomerular filtration rate (GFR) \>= 60 mL/min/1.73 m\^2 for subjects with creatinine levels \> 1.5 x institutional ULN, unless data exists supporting safe use at lower kidney function values, no lower than 30 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 * Patients with evidence of chronic hepatitis B virus (HBV) infection must have an undetectable viral load while 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 previously diagnosed brain metastases are eligible if they have completed their treatment and have recovered from the acute effects of radiation therapy or surgery prior to study enrollment, have discontinued corticosteroid treatment for these metastases for at least 2 weeks, and are neurologically stable. Patients with known symptomatic brain metastases requiring steroids are excluded. Of note, patients who required a single dose of corticosteroids on days receiving radiation treatment do not require a 2-week washout. Follow-up brain imaging after central nervous system (CNS)-directed therapy must show no evidence of progression and patient should be clinically stable for at least 1 month. This exception does not include carcinomatous meningitis, which is excluded regardless of clinical stability * 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. However, patients with concurrent malignancy that is progressing or requiring active treatment are excluded * 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. To be eligible for this trial, patients should be of class 2B or better * The effects of the combination ZEN003694 (ZEN-3694) and talazoparib on the developing human fetus are unknown. For this reason, and because 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 7 months after. 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 * 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 for 7 months after completion of study drug administration * Women of child-bearing potential MUST have a negative serum or urine human chorionic gonadotropin (HCG) test unless prior tubal ligation (\>/= 1 year before screening), total hysterectomy, or menopause (defined as 12 consecutive months of amenorrhea) * Ability to understand and the willingness to sign a written informed consent document

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Exclusion Criteria:

* Patients who are receiving any other investigational agents * History of allergic reactions attributed to compounds of similar chemical or biologic composition to ZEN003694 (ZEN-3694) or talazoparib * Patients receiving any medications or substances that are strong inhibitors or inducers of CYP3A4 or P-gp, strong inhibitors of BCRP, sensitive substrates of CYP1A2, proton-pump-inhibitors (H2 antagonists are allowed), and herbal medications/preparations (vitamins are allowed) are ineligible. Strong inhibitors or inducers of CYP3A4 must be discontinued at least 7 days prior to the first dose of ZEN003694 (ZEN-3694). 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. * Patients with uncontrolled intercurrent illness * Patients with psychiatric illness/social situations that would limit compliance with study requirements * Pregnant women are excluded from this study because ZEN003694 (ZEN-3694) is a BET inhibiting 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 (ZEN-3694), breastfeeding should be discontinued prior to the first dose of study drug and women should refrain from nursing throughout the treatment period and for 1 month following the last dose of the study drug. These potential risks may also apply to other agents used in this study * Patients who are involved in the planning and/or conduct of the study * Patients who are unable or unwilling to swallow pills * Active infection requiring intravenous (IV) antibiotics, or other uncontrolled intercurrent illness requiring hospitalization * Patients receiving any medications or substances that are factor Xa inhibitors (i.e., rivaroxaban, apixaban, betrixaban, edoxaban

otamixaban, letaxaban, eribaxaban) and factor IIa inhibitors (i.e., dabigatran). Low molecular weight heparin is allowed * Patients with radiation to \> 25% of the bone marrow * Patients who have had a bone-targeted radionuclide within 6 weeks of the first dose of ZEN003694 (ZEN-3694) or talazoparib * Patients who have previously received ZEN003694 (ZEN-3694) or who have been treated with an investigational BET inhibitor * Patients with cerebrovascular accident (CVA), myocardial infarction, or unstable angina within 6 months prior to the first dose of ZEN003694 (ZEN-3694) or talazoparib * Patients with impairment of gastrointestinal function that may significantly alter the absorption of ZEN003694 (ZEN-3694) or talazoparib * Patients that have had major surgery other than diagnostic surgery, dental surgery, or stenting within 4 weeks prior to the first dose of ZEN003694 (ZEN-3694) or talazoparib

Conditions & Interventions

Interventions:
DRUG: BET Bromodomain Inhibitor ZEN-3694, PROCEDURE: Biopsy Procedure, PROCEDURE: Biospecimen Collection, PROCEDURE: Diagnostic Imaging Testing, DRUG: Talazoparib
Conditions:
Advanced Malignant Solid Neoplasm, Metastatic Malignant Solid Neoplasm, Unresectable Malignant Solid Neoplasm

More Information

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