A Study Comparing the Combination of Pembrolizumab and Sacituzumab Govitecan Versus Standard of Care in the Treatment of Advanced Urothelial Cancer

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Patient must be ≥ 18 years of age * Patient must have Eastern Cooperative Oncology Group (ECOG) performance status 0-2. * Patient must have locally advanced (unresectable or not amenable to curative intent therapy) or metastatic urothelial cancer * Patient must have histologically proven conventional urothelial carcinoma (UC) of any urinary tract origin \[any histologic subtype except neuroendocrine (small or large cell)\] are permitted so long as tumors include ≥ 1% urothelial histology). NOTE: Pure non-urothelial histology is excluded * Patient must have measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria. Baseline imaging must be obtained ≤ 35 days prior to randomization * Patient must have the following prior treatment. Patient must have had progression on or after the immediate prior therapy * Patient must have had prior exposure to anti-PD(L)1 therapy \[anti -PD(L)1 monotherapy or as a combination regimen in any disease/therapy setting for UC. Patients must have received at least 1 dose of anti-PD(L)1 therapy * NOTE: Anti-PD(L)1 therapy does not need to be the most recent therapy received prior to enrollment on this protocol * Patient must not have had progression within 12 weeks of using anti-PD(l) 1 therapy * Patient must have had ≥ 1 line of systemic therapy given in the advanced/metastatic disease setting. For tumors with FGFR3 + susceptible alteration (for FGFR inhibitor), patients must have received a prior FGFR inhibitor unless contraindicated per physician discretion * Patient must have received prior enfortumab vedotin in any disease/therapy setting unless contraindicated per physician * Patient must have had no prior exposure to sacituzumab govitecan or other TROP-2 directed therapies or antibody-drug conjugate that contains topo-isomerase I inhibitor, e.g. trastuzumab deruxtecan * Patient must have Bellmunt score of 0-2. The Bellmunt score assesses a patient's risk and is calculated based upon ECOG PS, the hemoglobin level and presence of liver metastases * Patient must not have any history of grade 3 or higher immune-related adverse events on prior anti-PD1/L1, except for endocrinopathies on adequate hormone therapy repletion and clinically insignificant laboratory abnormalities * Patient must have recovered (i.e., ≤ grade 1) from clinically significant AEs due to previously administered systemic therapy agent, except for endocrinopathies on adequate hormone therapy repletion * NOTE: Patients with ≤ grade 2 neuropathy, any grade of alopecia, or any grade of non-clinically significant laboratory abnormality are exceptions to this criterion and are allowed in this trial. * Examples of non-clinically significant laboratory abnormalities include, but are not limited to: * Lymphopenia or monopenia * Lymphocytosis or monocytosis * Increase in amylase or lipase with no clinical correlation * Any other abnormal laboratory findings that have no clinical relevance per the treating investigators. * NOTE: If patient has undergone major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to randomization * Patient must not be pregnant or breast-feeding due to the potential harm to an unborn fetus and possible risk for adverse events in nursing infants with the treatment regimens being used. All patients of childbearing potential must have a blood test or urine study within 14 days prior to randomization to rule out pregnancy. A patient of childbearing potential is defined as anyone, regardless of whether they have undergone tubal ligation, who meets the following criteria: 1) has achieved menarche at some point, 2) has not undergone a hysterectomy or bilateral oophorectomy; or 3) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months). Patient must not nurse infants while on protocol treatment and for 4 months after the last dose of protocol treatment * Patient must not expect to conceive or father children by using an accepted and effective method(s) of contraception or by abstaining from sexual intercourse for the duration of their participation in the study. Patients of childbearing potential must continue contraceptive method(s) or abstain for 6 months after the last dose of protocol treatment. Patients with partners who could become pregnant should use effective contraception during therapy and for 3 months after the last dose of protocol treatment * Patient must have the ability to understand and the willingness to sign a written informed consent document. Patients with impaired decision-making capacity (IDMC) who have a legally authorized representative (LAR) or caregiver and/or family member available will also be considered eligible * Absolute neutrophil count (ANC) ≥ 1,500/uL (obtained ≤ 14 days prior to randomization) * Platelets ≥ 100,000/uL (obtained ≤ 14 days prior to randomization) * Albumin ≥ 3 g/dL (obtained ≤ 14 days prior to randomization) * Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN) (obtained ≤ 14 days prior to randomization) * Aspartate aminotransferase (AST)(serum glutamic oxaloacetic transaminase \[SGOT\]) and alanine aminotransferase (ALT)(serum glutamic pyruvic transaminase \[SGPT\]) ≤ 3 × institutional ULN or ≤ 5.0 x institutional ULN if known liver metastases (obtained ≤ 14 days prior to randomization) * Creatinine clearance (CrCl) ≥ 30 mL/min (obtained ≤ 14 days prior to randomization) NOTE: CrCl is estimated using the Cockcroft-Gault formula (or can be measured by 24-hour urine collection if needed) * Patient must not have a known genetic UGT1A1 deficiency (Gilbert's syndrome). Patients with variant type UGT1A1*28 allele may have increased levels of SN-38 metabolite (due to reduced SN-38 metabolism and clearance) and are at higher risk for severe adverse events when compared to wild-type. * NOTE: If a patient's UGT1A1 status is unknown, they are eligible to enroll (the study does not require this test as part of screening) * Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of randomization 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 considered 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 and are not using steroids \> 10 mg of prednisone (or equivalent) daily for brain metastases for at least 7 days prior to randomization * Patients with a prior or concurrent malignancy that is not considered clinically significant and whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen (at the discretion of the treating physician) are eligible for this trial * Patient must not be on systemic immunosuppressive medication, including steroids (if doses exceed the equivalent of prednisone 10 mg daily). Short courses of steroids, e.g. "burst", which are discontinued prior to randomization are acceptable. Patients on inhaled, intranasal, intra-articular and/or topical steroids are eligible * Patient must be English or Spanish speaking to be eligible for the HRQOL component of the study. * NOTE: Sites cannot translate the associated HRQOL forms

Conditions & Interventions

Interventions:

PROCEDURE: Biospecimen Collection, DRUG: Carboplatin, DRUG: Cisplatin, PROCEDURE: Computed Tomography, DRUG: Docetaxel, DRUG: Gemcitabine, PROCEDURE: Magnetic Resonance Imaging, DRUG: Paclitaxel, BIOLOGICAL: Pembrolizumab, OTHER: Questionnaire Administration, BIOLOGICAL: Sacituzumab Govitecan

Conditions:

Locally Advanced Urothelial Carcinoma, Metastatic Urothelial Carcinoma, Unresectable Urothelial Carcinoma

More Information

Contact(s): ctrrecruit@vcu.edu

Principal Investigator:

IRB

Number:
System ID: NCT06524544

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