Testing the Role of DNA Released From Tumor Cells Into the Blood in Guiding the Use of Immunotherapy After Surgical Removal of the Bladder, Kidney, Ureter, and Urethra for Urothelial Cancer Treatment, MODERN Study

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* PRE-REGISTRATION: Histologically confirmed muscle-invasive urothelial carcinoma of the urethra, bladder, ureter or renal pelvis * PRE-REGISTRATION: Variant histology, including neuroendocrine differentiation, sarcomatoid, micropapillary, glandular, trophoblastic, Mullerian, is allowed if urothelial cancer is predominant histology (any amount of squamous differentiation is allowed provided the tumor is not a pure squamous cell cancer) * PRE-REGISTRATION: Patient must have had radical surgery (i.e., cystectomy and lymph node dissection or nephroureterectomy or ureterectomy) ≥ 3 weeks, but ≤ 12 weeks prior to pre-registration. Patients who have had a partial cystectomy as definitive therapy are not eligible * PRE-REGISTRATION: No gross cancer at the surgical margins. Microscopic invasive urothelial carcinoma at the surgical margins (i.e., "positive margins") are allowed. Carcinoma in situ (CIS) at margins is considered negative margins * PRE-REGISTRATION: No evidence of residual cancer or metastasis after radical cystectomy or nephroureterectomy or ureterectomy (imaging is not required prior to pre-registration but is required prior to registration) * PRE-REGISTRATION: Have undergone a radical cystectomy nephroureterectomy, or ureterectomy with pathological evidence of urothelial carcinoma at high risk of recurrence as described in one of the two scenarios below (i or ii). The 7th edition of American Joint Committee on Cancer (AJCC) staging will be utilized.: * (i) Patients who have not received neoadjuvant systemic therapy: pT3-pT4* or pT0/x-pT4/N+ on radical surgery (i.e., cystectomy, nephroureterectomy, or ureterectomy) and are not eligible for adjuvant cisplatin chemotherapy * (i) Patients ineligible for cisplatin due to at least one of the following criteria and reason for ineligibility should be documented: * (i) Creatinine Clearance (using Cockcroft-Gault): \< 60 mL/min * (i) Common Terminology Criteria for Adverse Events (CTCAE) version 5, grade \>= 2 audiometric hearing loss * (i) CTCAE version 5, grade \>= 2 or above peripheral neuropathy * New York Heart Association Class III heart failure * (i) Eastern Cooperative Oncology Group (ECOG) performance status = 2 * (i) Patients who are eligible for cisplatin may be candidates if they refuse adjuvant cisplatin-based chemotherapy, despite being informed by the investigator about the treatment options. The patient's refusal must be documented. * (i) Patients with pT2N0 urothelial cancer on radical surgery specimen (without prior neoadjuvant systemic therapy) with ctDNA(+) Signatera results based on an assay performed post-radical surgery as part of routine care outside of the study may proceed with pre-registration but require confirmation of ctDNA(+) Signatera testing on repeat "central testing" in the context of A032103 testing. Patients with pT2N0 with central testing not confirming ctDNA(+) will not be eligible for A032103 (Note: this is distinct from patients with ypT2N0 who are eligible based on ii). * (ii) Patients who received neoadjuvant systemic therapy: ypT2-T4a and/or ypN+ on radical surgery (i.e., cystectomy. , nephroureterectomy, or ureterectomy) pathology specimen. Neoadjuvant systemic therapy may have included cisplatin-based chemotherapy, cisplatin-based chemotherapy plus PD-1/PD-L1 blockade, or enfortumab vedotin plus PD-1/PD-L1 blockade * PRE-REGISTRATION: Available tumor tissue for central Signatera testing to be submitted at pre-registration. Central testing is defined as testing performed as part of the A032103 study prior to registration and is provided by the study and not routine standard commercial testing. Patients who have already had local Signatera testing performed as part of routine care will require repeat central testing as part of the A032103 study to be eligible for registration/randomization. Tumor tissue from the radical surgery specimen is preferred over tissue from prior diagnostic biopsy specimen (e.g., transurethral resection of bladder tumor specimen) * PRE-REGISTRATION: Age \>= 18 years * PRE-REGISTRATION: ECOG Performance Status 0-2 * PRE-REGISTRATION: Not pregnant and not nursing, because this study involves an agent that has known genotoxic, mutagenic and teratogenic effects * PRE-REGISTRATION: No postoperative/adjuvant systemic therapy after radical surgery * PRE-REGISTRATION: No adjuvant radiation after radical surgery * PRE-REGISTRATION: No treatment with any other type of investigational agent =\< 4 weeks before pre-registration * PRE-REGISTRATION: Not have ever received prior treatment with LAG-3 blockade * PRE-REGISTRATION: 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 * PRE-REGISTRATION: Absolute Neutrophil Count (ANC) \>= 1,200/mm\^3 * PRE-REGISTRATION: Platelet count \>= 100,000/mm\^3 * PRE-REGISTRATION: Hemoglobin \>= 8 g/dL * PRE-REGISTRATION: Creatinine =\< 1.5 x upper limit of normal (ULN) or calculated (calc.) creatinine clearance \> 30 mL/min (using either Cockcroft-Gault formula or Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation * PRE-REGISTRATION: Aspartate aminotransferase (AST)/alanine aminotransferase (ALT) =\< 3 x ULN * PRE-REGISTRATION: Total bilirubin =\< 1.5 x upper limit of normal (ULN) (except in patients with Gilbert Syndrome, who can have total bilirubin \< 3.0 mg/dL) * PRE-REGISTRATION: For women of childbearing potential only: A negative urine or serum pregnancy test done =\< 14 days prior to pre-registration is required * PRE-REGISTRATION: Not currently requiring hemodialysis * PRE-REGISTRATION: No current or prior history of myocarditis * PRE-REGISTRATION: No grade ≥ 3 immune related adverse event with prior PD-1/PD-L1 blockade * PRE-REGISTRATION: No active autoimmune disease or history of autoimmune disease that might recur, which may affect vital organ function or require immune suppressive treatment including systemic corticosteroids. These include but are not limited to patients with a history of immune related neurologic disease, multiple sclerosis, autoimmune (demyelinating) neuropathy, Guillain-Barre syndrome, myasthenia gravis; systemic autoimmune disease such as systemic lupus erythematosus (SLE), connective tissue diseases, scleroderma, inflammatory bowel disease (IBD), Crohn's, ulcerative colitis, hepatitis; and patients with a history of toxic epidermal necrolysis (TEN), Stevens- Johnson syndrome, or phospholipid syndrome because of the risk of recurrence or exacerbation of disease. * PRE-REGISTRATION: Patients with vitiligo, endocrine deficiencies including type I diabetes mellitus, thyroiditis managed with replacement hormones including physiologic corticosteroids are eligible. * PRE-REGISTRATION: Patients with rheumatoid arthritis and other arthropathies, Sjögren's syndrome and psoriasis controlled with topical medication and patients with positive serology, such as antinuclear antibodies (ANA), anti-thyroid antibodies should be evaluated for the presence of target organ involvement and potential need for systemic treatment but should otherwise be eligible. * PRE-REGISTRATION: No current pneumonitis or prior history of non-infectious pneumonitis that required steroids within the previous 5 years. * PRE-REGISTRATION: No known active hepatitis B (e.g., hepatitis B surface antigen \[HBsAg\] reactive) or hepatitis C (e.g., hepatitis C virus \[HCV\] ribonucleic acid \[RNA\] \[qualitative\] is detected). * PRE-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. * PRE-REGISTRATION: Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible. * PRE-REGISTRATION: No concurrent antineoplastic therapy. * PRE-REGISTRATION: No current immunosuppressive agents (with the exception of corticosteroids as described below). * PRE-REGISTRATION: No condition requiring systemic treatment with either corticosteroids (\> 10 mg daily prednisone equivalents) or other immunosuppressive medications within 14 days of pre-registration (with the exception of steroid pre-medications for contrast allergies). Inhaled or topical steroids and adrenal replacement doses \< 10 mg daily prednisone equivalents are permitted in the absence of active autoimmune disease. * REGISTRATION: Patient must have had radical cystectomy and lymph node dissection or nephroureterectomy or ureterectomy =\< 18 weeks prior to registration. * REGISTRATION: Must have evaluable ctDNA Signatera assay result (i.e., ctDNA\[+\]or ctDNA\[-\]) based on test performed as part of central testing at pre-registration to A032103. Central testing is defined as testing performed as part of the A032103. Local/commercial testing results may not be used for registration to A032103 * Cisplatin-ineligible (or cisplatin-declining) patients with a pT2N0 urothelial cancer on cystectomy or nephroureterectomy or ureterectomy who were pre-registered based on routine standard care ctDNA(+) Signatera testing must have confirmed ctDNA(+) Signatera testing on central testing. If central Signatera testing yields a ctDNA(-) result, these patients are ineligible. NOTE: This is a distinct consideration from patients with ypT2-4 and/or ypN+ urothelial cancer (i.e., patients who had received neoadjuvant cisplatin-based

are ineligible. NOTE: This is a distinct consideration from patients with ypT2-4 and/or ypN+ urothelial cancer (i.e., patients who had received neoadjuvant cisplatin-based chemotherapy) who are eligible with either ctDNA(+) or ctDNA(-) central Signatera testing * REGISTRATION: All patients must have confirmed disease-free status defined as no measurable disease by Response Evaluation Criteria in Solid Tumors (RECIST) 1.1, or definitive non-measurable radiographic metastatic disease, within 60 days prior to registration. Patients with equivocal nodes less than 15 mm in short axis, or \< 10 mm in long axis for non-lymph node lesions, not considered by the investigator to represent malignant disease will be eligible. Attempts should be made to resolve the etiology of equivocal lesions with complementary imaging (e.g., PET scan) or biopsy. * REGISTRATION: No major surgery =\< 3 weeks before registration. * REGISTRATION: No live vaccine within 30 days prior to registration. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, Bacillus Calmette- Guerin (BCG), and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines (e.g., FluMist \[registered trademark\]) are live attenuated vaccines and are not allowed. Coronavirus disease 2019 (COVID-19) vaccines are not live vaccines and are allowed * REGISTRATION: No change since registration in clinical condition and/or laboratory tests that would impact the safety of nivolumab +/- relatlimab administration in the opinion of the treating investigator * COHORT B, ARM 4 PATIENTS INITIATING NIVOLUMAB AFTER CONVERSION OF ctDNA ASSAY FROM ctDNA(-) to ctDNA (+): * Patient must have converted to ctDNA(+) during serial monitoring performed centrally in the setting of the A032103 study * COHORT B, ARM 4 PATIENTS INITIATING NIVOLUMAB AFTER CONVERSION OF ctDNA ASSAY FROM ctDNA(-) to ctDNA (+): * No evidence of metastatic disease on the most recent scheduled imaging assessment as outlined in the study calendar (no repeat imaging is necessary specifically at the time of the conversion from ctDNA\[-\] to ctDNA\[+\]). * COHORT B, ARM 4 PATIENTS INITIATING NIVOLUMAB AFTER CONVERSION OF ctDNA ASSAY FROM ctDNA(-) to ctDNA (+): * No change in clinical condition and/or laboratory tests that would impact the safety of nivolumab administration in the opinion of the treating investigator * COHORT B, ARM 4 PATIENTS INITIATING NIVOLUMAB AFTER CONVERSION OF ctDNA ASSAY FROM ctDNA(-) to ctDNA (+): * =\< 6 weeks from reporting of ctDNA(+) result to site (not from the date sample was drawn).

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, OTHER: cfDNA or ctDNA Measurement, PROCEDURE: Computed Tomography, PROCEDURE: Cystoscopy, PROCEDURE: Magnetic Resonance Imaging, BIOLOGICAL: Nivolumab, OTHER: Questionnaire Administration, BIOLOGICAL: Relatlimab
Conditions:
Muscle Invasive Bladder Urothelial Carcinoma, Muscle Invasive Renal Pelvis Urothelial Carcinoma, Muscle Invasive Ureter Urothelial Carcinoma, Muscle Invasive Urethral Urothelial Carcinoma, Stage II Bladder Urothelial Carcinoma AJCC v6 and v7, Stage III Bladder Urothelial Carcinoma AJCC v6 and v7, Stage IV Bladder Urothelial Carcinoma AJCC v7

More Information

Contact(s): ctrrecruit@vcu.edu
Principal Investigator:
Phase: PHASE2
IRB
Number:
System ID: NCT05987241
