Personalized Antibody-Drug Conjugate Therapy Based on RNA and Protein Testing for the Treatment of Advanced or Metastatic Solid Tumors (The ADC MATCH Screening and Treatment Trial)

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* SCREENING PROTOCOL INCLUSION CRITERIA: * Patients must have histologically confirmed solid tumor requiring therapy and meet one of the following criteria: * Patients must have disease not amenable to curative-intent therapy OR * Patients who have had disease progression after treatment with all available therapies for their disease that are known to confer benefit or are intolerant to such treatment will be eligible, if other eligibility criteria are met. If the patient is currently receiving therapy without progression, the clinician must have assessed that the current therapy is no longer benefitting the patient, or that the patient is not tolerating the therapy. Patients can be screened on ADC MATCH if they are on first-line treatment and expected to need a treatment change within 3 months, and ADC MATCH is felt to be appropriate next line therapy OR * Patients with disease for which no standard treatment exists that has been shown to confer benefit OR * Patients who are willing to forego standard therapies known to confer benefit * NOTE: Patients can be on therapy at the time of initiating the Screening Protocol if the patient is interested in treatment on ADC MATCH upon progression, and the physician deems this appropriate * Patient must have undergone RNA testing in a Clinical Laboratory Improvement Act (CLIA) environment. Patients who have high TOI RNA expression will have confirmation of TOI expression by CLIA IHC assay at MD Anderson Cancer Center (MDACC). Only patients with confirmed TOI protein expression will be eligible for assignment to a treatment cohort. Retrospective confirmation in another central laboratory may also be performed * Patients must be willing to undergo mandatory pre-treatment and on-treatment tumor biopsies. Patients who do not consent to these research biopsies will not be eligible for prescreening. Patients who have screened and consented to a treatment cohort but are found to have disease that cannot be safely biopsied will be eligible for treatment provided all other eligibility criteria are met * Patients must have measurable disease * Age ≥ 18 years. Because no dosing or adverse event (AE) data are currently available on the use of the Cancer Therapy Evaluation Program (CTEP) investigational new drug (IND) agents to be used in the study in patients \< 18 years of age, children are excluded from this study * Eastern Cooperative Oncology Group performance status of 0-2 (Karnofsky ≥ 50%) * No history of transfusion dependence * No history of persistent bone marrow suppression (absolute neutrophil count ≥ 1,500/mL and platelets ≥ 100,000/mL not attributable to active therapy; patients currently on bone marrow suppressive therapy can undergo assessment for the screening protocol but cannot be treated on any of the treatment cohorts unless bone marrow suppression is reversed off the suppressive therapy) * Total bilirubin ≤ 1.5 institutional upper limit of normal (ULN). Documented Gilbert syndrome is allowed if total bilirubin is ≤ 3 × ULN * Aspartate transaminase (serum glutamic-oxaloacetic transaminase \[SGOT\])/alanine transaminase (serum glutamate pyruvate transaminase \[SGPT\]) ≤ 2.5 × institutional ULN. Transaminases up to 5 × ULN in the presence of liver metastases are not allowed to initiate the screening protocol but are allowed for the treatment cohorts * Creatinine ≤ institutional ULN OR glomerular filtration rate ≥ 60 mL/min/1.73 m\^2 for patients with creatinine levels above institutional normal unless data exists supporting safe use at lower kidney function values, no lower than 30 mL/min/1.73 m\^2 * Patients must have albumin ≥ 3 g/dL * Human immunodeficiency virus-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this study * 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 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 agents are eligible for this study * 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 study, patients should be class 2B or better * Women of childbearing potential must have a negative human serum pregnancy test result at the screening protocol * The effects of the study drugs on the developing human fetus are unknown. For this reason and because investigational agents as well as other therapeutic agents used in this trial are known to be teratogenic, women of childbearing 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 6 months after completion of study drug administration (unless otherwise indicated in the eligibility section of the treatment cohort protocols). 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 study entry, for the duration of study participation, and for 6 months after completion of study drug administration * Ability to understand and the willingness to sign a written informed consen document * ADDITIONAL INCLUSION CRITERIA FOR TREATMENT COHORTS: * Women of childbearing potential must have a negative serum pregnancy test result at treatment cohort screening * Hemoglobin \> 9.0 g/dL * Leukocytes ≥ 3000/mL * Absolute neutrophil count ≥ 1,500/mL * Platelets ≥ 100,000/mL * Patient must be willing to sign the relevant treatment cohort consent form * COHORT A INCLUSION CRITERIA: * Patients must fulfill all the eligibility criteria outlined in the ADC MATCH screening protocol at the time of treatment cohort A registration * Patient must have high Trop-2 protein expression (IHC 2+ or 3+) as determined by the MD Anderson Cancer Center Clinical Laboratory Improvement Amendments IHC assay * Patients who have Trop-2 IHC testing without RNA testing or who have Trop-2 IHC 2 or 3+ expression but do not have Trop-2 expression detected on RNA testing will not be eligible for the trial. * Patients who have Trop-2 RNA expression and Trop-2 IHC 2+ or 3+ on another Trop-2 IHC test will undergo Trop-2 testing with the integral MDACC IHC assay * Patients who already have RNA expression testing demonstrating Trop-2 RNA expression as well as IHC testing on the MDACC CLIA lab platform will be eligible for enrollment after review of results by the Precision Oncology Decision Support team without having to repeat Trop-2 IHC results as part of pre-screening. Patients who have had TROP2 2+ testing result performed outside of MDACC will have to undergo MDACC TROP2 IHC analysis before enrollment * COHORT B INCLUSION CRITERIA: * Patients must fulfill all the eligibility criteria outlined in the ADC MATCH screening protocol at the time of treatment cohort B registration * Patient must have high Nectin-4 protein expression (IHC 2+ or 3+) as determined by the MD Anderson Cancer Center Clinical Laboratory Improvement Amendments IHC assay * COHORT C INCLUSION CRITERIA: * Patients must fulfill all the eligibility criteria outlined in the ADC MATCH screening protocol at the time of treatment cohort C registration * Patient must have HER2 protein expression (IHC 2+ or 3+) as determined by the MD Anderson Cancer Center (MDACC) IHC assay * Patients who have HER2 IHC testing without RNA testing or who have HER2 IHC 2 or 3+ expression but do not have HER2 expression detected on RNA testing will not be eligible for the trial * Patients who have HER2 RNA expression and HER2 IHC 3+ or 2+ on another HER2 IHC test will undergo HER2 testing with the integral MDACC IHC assay * Patients who already have RNA expression testing demonstrating HER2 RNA expression as well as IHC testing on the MDACC CLIA lab platform will be eligible for enrollment after review of results by the Precision Oncology Decision Support team without having to repeat HER2 IHC results as part of pre-screening. Patients who have had HER2 2+ testing result performed outside of MDACC will have to undergo MDACC HER2 IHC analysis before enrollment * Women of childbearing potential 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 completion of study drug administration. Women should not breastfeed during the study treatment period and for 7 months after completion of study drug administration. 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 study entry, for the duration of study participation, and for 4 months after completion of study drug administration. Female patients must not donate, or retrieve for their own use, ova from the time of screening throughout the study treatment period and for at least 7 months after the final study drug administration. Female patients may wish to consider preservation of ova prior to enrollment in the study. Male patients should refrain from freezing or donating sperm

administration * Female patients may wish to consider preservation of ova prior to enrollment in the study. Male patients should refrain from freezing or donating sperm during the study and for 6 months after the final study drug administration. Preservation of sperm should be considered prior to enrollment in the study * LVEF ≥50% within 28 days before enrollment

Exclusion Criteria:

* SCREENING PROTOCOL EXCLUSION CRITERIA: * Patients with new or progressive brain metastases (active brain metastases) or leptomeningeal disease. Patients with treated brain metastases are eligible if follow-up brain imaging 4 weeks after central nervous system-directed therapy shows no evidence of progression * Clinically significant cardiovascular condition including: (1) history of congestive heart failure (New York Health Association class \> 2), (2) any history of unstable angina, (3) myocardial infraction within the past 12 months, or (4) any history of supraventricular arrhythmia or ventricular arrhythmia requiring treatment or intervention * History or presence of abnormal electrocardiogram (ECG) that, in the investigator's opinion, is clinically meaningful * Active or chronic corneal disorder including, but not limited to, Sjogren's syndrome, Fuchs corneal dystrophy (requiring treatment), history of corneal transplantation, active herpetic keratitis, and/or active ocular conditions requiring ongoing treatment/monitoring such as wet age-related macular degeneration requiring intravitreal injections, active diabetic retinopathy with macular edema, presence of papilledema, and acquired monocular vision * History of allergic reactions attributed to compounds of similar chemical or biologic composition to the ADCs used in the study * History of interstitial lung disease or pneumonitis requiring steroid therapy * Grade 2 or greater peripheral neuropathy * Patients requiring the use of full dose coumarin-derivative anticoagulants such as warfarin. Low molecular weight heparin is permitted for prophylactic or therapeutic use. Factor X inhibitors are permitted * Note: Warfarin may not be started while enrolled in the treatment cohorts. Stopping the anticoagulation for biopsy should be per site standard operating practice * Pregnant women are excluded from the study because the study drugs are investigational or approved agents with the potential for teratogenic or abortifacient effects. Because there is an unknown but potential risk for AEs in nursing infants secondary to treatment of the mother with any of the study drugs, breastfeeding should be discontinued if the mother is treated with any of the study drug * ADDITIONAL EXCLUSION CRITERIA FOR TREATMENT COHORTS: * Patients must have adequate washout from prior therapy at the time of study treatment initiation: 4 weeks from major surgery; 4 weeks from antibody-based therapy; 2 weeks or 5 half-lives (whichever is shorter) from any targeted therapy or small molecule therapy; 3 weeks or 5 half-lives (whichever is shorter) from chemotherapy or 6 weeks in the case of certain therapies (e.g., extensive radiotherapy, mitomycin C, and nitrosoureas); and 4 weeks from radiation therapy. Patients should have received no more than 3 prior lines of chemotherapy. Testosterone suppression as supportive treatment for castration-resistant prostate cancer and ovarian suppression in premenopausal patients with breast cancer that have supportive treatment and not anticancer treatment role (with luteinizing hormone-releasing hormone analogs) will be allowed if the patients were on these supportive treatments before starting the study. Use of bone-modifying medications (bisphosphonates or denosumab) will be allowed. Palliative radiotherapy of non-target lesions is permitted, but presence of new or worsening metastases will be considered progressive disease. If there is clear evidence of clinical benefit, study treatment may be continued 2 weeks after completion of palliative radiotherapy to lesions that are non-target lesions. Patients can be on therapy during treatment cohort screening * Patients who are currently receiving any other investigational agent(s) * Received systemic therapy with corticosteroids at \> 20 mg/day prednisone or equivalent within 1 week prior to cycle 1 day 1 * Patients who have not recovered from AEs due to prior anticancer therapy (i.e., have residual toxicities \> grade 1) with the exception of alopecia * When the corrected QT interval (QTc) by Fridericia's formula is \< 120 ms, \> 450 ms in males and \> 470 ms in females. When the QTc by Rautaharju's formula is ≥ 120 ms, \> 450 ms in males and \> 470 ms in females * Uncontrolled infection requiring intravenous antibiotic, antiviral, or antifungal use * Received a live, attenuated vaccine within 30 days prior to cycle 1 day 1. Enrolled patients should not receive live vaccine during the study. Non-live COVID vaccines will be allowed on study, but it is recommended to avoid their use during the first treatment cycle (from 3 days prior to cycle 1 day 1 through cycle 2 day 3) * Patients with uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements * Other concurrent medical or psychiatric conditions that, in the investigator's opinion, may be likely to confound study interpretation or prevent completion of study procedures and follow-up examinations * COHORT A EXCLUSION CRITERIA: * Patients with histologically documented advanced colorectal cancer, urothelial cancer, head and neck cancer, triple negative breast cancer (TNBC), HR-positive breast cancer, HER2-positive breast cancer, small cell lung cancer, NSCLC, and endometrial cancer * Patients who have received growth factor support within 2 weeks of study treatment initiation * Coadministration of sacituzumab govitecan (IMMU-132) with inhibitors of UGT1A1 may increase systemic exposure to the active metabolite, SN-38. UGT1A1 inhibitors should not be administered concomitantly with sacituzumab govitecan (IMMU-132) unless there are no therapeutic alternatives * Prior topoisomerase 1 inhibitor treatment * Prior treatment with a Trop-2-targeting ADC * Has active chronic inflammatory bowel disease (ulcerative colitis, Crohn's disease) or gastrointestinal (GI) perforation within 6 months of treatment cohort A registration * COHORT B EXCLUSION CRITERIA: * Patients with histologically documented advanced urothelial cancer, head and neck cancer, breast cancer, lung cancer, gastric cancer, gastroesophageal junction cancer, esophageal cancer, prostate cancer, or penile cancer * Concomitant use of strong inhibitors or strong inducers of cytochrome P450 (CYP)3A4. Washout period is 2 weeks prior to study treatment initiation * History of uncontrolled diabetes mellitus within 3 months before the first dose of study treatment. Uncontrolled diabetes mellitus is defined as hemoglobin A1c ≥ 8% or hemoglobin A1c between 7 and \< 8% with associated diabetes symptoms (polyuria or polydipsia) that are not otherwise explained * Known active keratitis or corneal ulcerations. Patients with superficial punctate keratitis are allowed if the disorder is being adequately treated * Known hypersensitivity to enfortumab vedotin or to any excipient in the drug formulation of enfortumab vedotin (including histidine, trehalose dihydrate, and polysorbate 20), or known hypersensitivity to biopharmaceutical produced in Chinese hamster ovary cells * Prior treatment with an ADC with vedotin payload * COHORT C EXCLUSION CRITERIA: * Patients with histologically documented advanced breast cancer, non-small cell lung cancer (NSCLC), colorectal carcinoma (CRC), gastric cancer, or gastroesophageal junction (GEJ) cancer * Previous treatment with topoisomerase I inhibitors as a free form or as other formulations, and ADCs with topoisomerase I inhibitor payloads * Patients receiving treatment with chloroquine or hydroxychloroquine are not allowed to participate in the study, unless there is a washout period of at least 14 days prior to the first dose of study drug * History of non-infectious pneumonitis/interstitial lung disease (ILD), current ILD, or where suspected ILD that cannot be ruled out by imaging at screening * Lung-specific intercurrent clinically significant illnesses including, but not limited to, any underlying pulmonary disorder (i.e., pulmonary emboli within 3 months of initiation of study drug, severe asthma, severe chronic obstructive pulmonary disease, restrictive lung disease, pleural effusion etc.) * Any autoimmune, connective tissue or inflammatory disorders (e.g., Rheumatoid arthritis, Sjogren's, sarcoidosis etc.) where there is documented, or a suspicion of pulmonary involvement at the time of screening * Prior pneumonectomy * History of severe hypersensitivity reactions to other monoclonal antibodies

Conditions & Interventions

Interventions:
PROCEDURE: Biopsy Procedure, PROCEDURE: Biospecimen Collection, PROCEDURE: Computed Tomography, PROCEDURE: Echocardiography Test, OTHER: Electronic Health Record Review, DRUG: Enfortumab Vedotin, OTHER: Immunohistochemistry Staining Method, PROCEDURE: Magnetic Resonance Imaging, PROCEDURE: Multigated Acquisition Scan, BIOLOGICAL: Sacituzumab Govitecan, BIOLOGICAL: Trastuzumab Deruxtecan
Conditions:
Advanced Malignant Solid Neoplasm, Metastatic Malignant Solid Neoplasm

More Information

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