Testing Teclistamab (TECVAYLI) in Combination With Iberdomide for Relapsed or Refractory Multiple Myeloma

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Patients must have histologically or cytologically confirmed multiple myeloma (MM), as defined in the International Myeloma Working Group (IMWG) criteria * If patients have undergone autologous stem cell transplant (SCT), day 0 of SCT must be \> 100 days to be eligible for the study * Patients must have had disease progression after ≥ 4 prior lines of anti-myeloma treatments including one proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib), one immunomodulatory imide drug (ImiD) (e.g., thalidomide, lenalidomide, pomalidomide \[POM\]), and one anti-CD38 monoclonal antibody (e.g., daratumumab, isatuximab) * Patients must have measurable disease, defined as: * Serum M-protein ≥ 0.5 g/dL (≥ 5 g/L) * Urine M-protein ≥ 200 mg/24 h * Serum free light chain (FLC) assay: "involved" FLC level ≥ 10 mg/dL (≥ 100 mg/L) and an abnormal serum free light chain ratio (\< 0.26 or \> 1.65) * Note: Patients with non-secretory disease will be allowed to participate * Age ≥ 18 years * Because no dosing or adverse event data are currently available on the use of iberdomide in combination with teclistamab in patients \< 18 years of age, children are excluded from this study * Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 (Karnofsky ≥ 60) * Hemoglobin ≥ 7.0 g/dL (≤ 28 days prior to registration) (Without growth factor support, blood transfusion, or platelet stimulating agents for the past 7 days, excluding erythropoietin) * Absolute neutrophil count ≥ 1,000/mcL (≤ 28 days prior to registration) (Without growth factor support, blood transfusion, or platelet stimulating agents for the past 7 days, excluding erythropoietin) * Platelets ≥ 50,000/mcL (≤ 28 days prior to registration) (Without growth factor support, blood transfusion, or platelet stimulating agents for the past 7 days, excluding erythropoietin) * Total bilirubin ≤ 2 x institutional upper limit of normal (ULN) (≤ 28 days prior to registration) * Aspartate aminotransferase (AST)(serum glutamic oxaloacetic transaminase \[SGOT\])/alanine aminotransferase (ALT)(serum glutamic pyruvic transaminase \[SGPT\]) ≤ 3 x institutional ULN (≤ 28 days prior to registration) * Estimated glomerular filtration rate (eGFR) \> 30 mL/min (≤ 28 days prior to registration) * Spot urine (albumin/creatine ratio) ≤ 500mg/g (56 mg/mmol) OR urine dipstick negative/trace (if \> 1+ only eligible if confirmed ≤ 500 mg/g (56 mg/mmol) by albumin/creatinine ratio (spot urine from first void) (≤ 28 days prior to registration) * Note: Laboratory results obtained during screening should be used to determine eligibility criteria. In situations where laboratory results are outside the permitted range, the investigator may re-test the subject and the subsequent within range screening result may be used to confirm eligibility * Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months 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 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 done a minimum of 28 days after completion of central nervous system (CNS)-directed therapy shows no evidence of progression * Patients with new or progressive brain metastases (active brain metastases) or leptomeningeal disease are eligible if the treating physician determines that immediate CNS specific treatment is not required and is unlikely to be required during the first cycle of therapy * 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 * 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 class II or better * Based on the mechanism of action, teclistamab may cause fetal harm when administered to a pregnant woman. Females of child-bearing potential (FCBP): should use effective contraception during treatment with teclistamab and for 5 months after the last dose. FCBP should not breast feed during treatment with teclistamab and for 5 months after the last dose. Should a FCBP become pregnant or suspect she is pregnant while she or her partner is participating in this study, she should inform her treating physician immediately. The effects of iberdomide on the developing human fetus are unknown. However, IMiDs are known to be teratogenic. FCBP must have a negative serum or urine pregnancy test with a sensitivity of at least 25 mIU/mL within 10-14 days prior to starting iberdomide, and again within 24 hours. FCBP must either commit to continued abstinence from heterosexual intercourse or begin two acceptable methods of birth control-one highly effective method and one additional effective method-at the same time, at least 28 days before starting iberdomide, while taking iberdomide, and for 28 days following discontinuation from the study. Examples of highly effective methods are intrauterine device, hormonal contraceptives, tubal ligation, or partner's vasectomy. Examples of barrier method are male condom, diaphragm, or cervical cap. FCBP must also agree to ongoing pregnancy testing. Men must practice complete abstinence or agree to use a condom during sexual contact with FCBP while participating in the study, during dose interruptions, and for at least 28 days following discontinuation from the study, even if he has undergone a successful vasectomy. All patients must be counseled at a minimum of every 28 days about pregnancy precautions and risk of fetal exposure * Men must agree to abstain from donating and semen or sperm while taking iberdomide, during dose interruptions, and for at least 28 days after the last dose of iberdomide. FCBP must agree not to donate eggs (ova, oocytes) for the purpose of reproduction during this period * All patients must agree to abstain from donating blood products while taking iberdomide and for at least 28 days after the last dose of iberdomide * Ability to understand and the willingness to sign a written informed consent document. Legally authorized representatives may sign and give informed consent on behalf of study subjects * Willingness to adhere to the study visit schedule and other protocol requirements and provide mandatory blood and bone marrow specimens for correlative research * Willingness to return to the enrolling institution for follow-up

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Exclusion Criteria:

* Patients who have active plasma cell leukemia, active amyloid light chain (AL) (primary) amyloidosis, active polyneurophathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes (POEMS) syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma proliferative disorder, myeloma protein, and skin changes), and Waldenstrom macroglobulinemia are ineligible * If a patient develops recurrent/refractory (R/R) disease while receiving the most recent line of therapy, there is no need for a washout period * Patients who have had prior anti-BCMA directed bispecific antibody (BsAb) therapy exposure (prior treatment with anti-BCMA directed antibody drug conjugate, anti-BCMA-directed chimeric antigen receptor (CAR) T cell therapy, and prior non-BCMA-targeting BsAb are permitted) * Patients who have had prior treatment with a cereblon E3 ligase modulator, including mezigdomide, iberdomide, and CFT7455 (all currently in clinical development) * Patients who received plasmapheresis ≤ 7 days prior to registration * Patients who received a prior allogeneic stem cell transplant. Autologous SCT is allowed * Patients who received a live or live-attenuated vaccine ≤ 30 days prior to registration. Patients are allowed to receive a COVID-19 vaccine at any timepoint during protocol treatment * Systemic active infection requiring treatment * Any unresolved toxicity ≥ grade 2 from previous treatment except for alopecia or peripheral neuropathy up to grade 2 * Patients who have had any major surgery ≤ 4 weeks prior to registration * Patients with uncontrolled intercurrent illness or any other significant condition(s) that would make this protocol unreasonably hazardous * Patients with evidence of active mucosal or internal bleeding * Current unstable liver or biliary disease per investigator assessment defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminemia, esophageal or gastric varices, persistent jaundice, or cirrhosis. Stable chronic liver disease (including Gilbert's syndrome or asymptomatic gallstones) or hepatobiliary involvement of malignancy is acceptable if participant otherwise meets entry criteria * Patients with known immediate or delayed hypersensitivity reaction or idiosyncratic reaction to drugs chemically related to teclistamab or iberdomide, or any of the components of the study treatment * Patients who are taking any anticancer therapy other than hormonal therapy (for prostrate or breast cancer) and palliative radiotherapy (defined as radiation to ≤ 3 sites of active multiple myeloma) * Patients who require immunosuppressive medications including, but

not limited to, systemic corticosteroids at doses exceeding 10 mg/day of prednisone or equivalent. Use of immunosuppressive medications for the management of iberdomide-related adverse events (AEs) or in subjects with contrast allergies is acceptable. In addition, use of inhaled, topical, intranasal corticosteroids or local steroid injection (e.g., intra-articular injection) is permitted. Temporary use of corticosteroids for concurrent illnesses (e.g., food allergies, computed tomography \[CT\] scan contrast hypersensitivity, pneumonia, etc.) are acceptable * Patients who require medications that are strong inhibitors or inducers of CYP3A4/5 * Patients who are receiving any other investigational agents * Patients with uncontrolled intercurrent illness or any other significant condition(s) that would make participation in this protocol unreasonably hazardous * Pregnant women are excluded from this study because iberdomide is a thalidomide analog and thalidomide is a known human teratogen. Because there is an unknown but potential risk for adverse events in nursing infants secondary to treatment of the mother with iberdomide, breastfeeding should be discontinued if the mother is treated with iberdomide. These potential risks may also apply to other agents used in this study * Patients who are unable or unwilling to undergo protocol required thromboembolism prophylaxis are excluded

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Marrow Aspiration, PROCEDURE: Bone Marrow Biopsy, PROCEDURE: Computed Tomography, DRUG: Iberdomide, PROCEDURE: Magnetic Resonance Imaging, PROCEDURE: Positron Emission Tomography, DRUG: Teclistamab
Conditions:
Recurrent Multiple Myeloma, Refractory Multiple Myeloma

More Information

Contact(s): ctrrecruit@vcu.edu
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