Testing the Combination of an Anti-cancer Drug, Iadademstat, With Other Anti-cancer Drugs (Atezolizumab or Durvalumab) at Improving Outcomes for Small Cell Lung Cancer

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 small cell lung cancer (SCLC) * Patients who have been treated with platinum etoposide chemotherapy plus either atezolizumab or durvalumab immunotherapy for at least 4 cycles, and no more than 6 cycles, with either a radiographic response or stable disease. Patients are eligible if a maximum of 2 cycles of atezolizumab or durvalumab were omitted with initial treatment * Age ≥ 18 years. Because no dosing or adverse event data are currently available on the use of iadademstat in combination with atezolizumab and durvalumab in patients \<18 years of age, children are excluded from this study * Body weight ≥ 50 kg * Patient is able to swallow oral medications * Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 (Karnofsky ≥ 60%). This assessment for eligibility will take place after patients have received 4 cycles of standard of care (SOC) chemotherapy-ICI * Leukocytes ≥ 2,000/mcL * Lymphocyte count ≥ 500/mcL * Absolute neutrophil count ≥ 1,500/mcL * Hemoglobin ≥ 9 g/dL * Platelets ≥ 100,000/mcL * Albumin ≥ 3 g/dL * Total bilirubin ≤ 1.5 institutional upper limit of normal (ULN) * Aspartate aminotransferase (AST)(serum glutamic oxaloacetic transaminase \[SGOT\])/ alanine aminotransferase (ALT) (serum glutamic pyruvic transaminase \[SGPT\]) ≤ 3 × institutional ULN unless liver metastases are present, in which case it must be ≤ 5 × ULN * Glomerular filtration rate (GFR) ≥ 45 mL/min * 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 (no escalating steroid use) untreated brain metastases (≤ 5 mm without significant edema) are eligible. Brain metastases must not be new after completion of chemotherapy * 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 * Evidence of post-menopausal status or negative urinary or serum pregnancy test for female pre-menopausal patients. Pregnant women are excluded from this study because atezolizumab and durvalumab are monoclonal antibody agents with the potential for teratogenic or abortifacient effects. Women will be considered post-menopausal if they have been amenorrheic for 12 months without an alternative medical cause. The following age-specific requirements apply: * Women \< 50 years of age would be considered post-menopausal if they have been amenorrheic for 12 months or more following cessation of exogenous hormonal treatments and if they have luteinizing hormone and follicle-stimulating hormone levels in the post-menopausal range for the institution or underwent surgical sterilization (bilateral oophorectomy or hysterectomy). * Women ≥ 50 years of age would be considered post-menopausal if they have been amenorrheic for 12 months or more following cessation of all exogenous hormonal treatments, had radiation-induced menopause with last menses \>1 year ago, had chemotherapy-induced menopause with last menses \> 1 year ago, or underwent surgical sterilization (bilateral oophorectomy, bilateral salpingectomy or hysterectomy) * The effects of iadademstat, atezolizumab, and durvalumab on the developing human fetus are unknown. For this reason and because monoclonal antibody agents are known to be teratogenic, women of child-bearing potential and males with females of child-bearing potential must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to registration, for the duration of study participation, and for 150 days after the last dose of study medication. 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. * Females of childbearing potential must agree to: * Use effective contraception during the trial and 150 days after the end of treatment. * Practice true abstinence during the trial and 150 days after the end of treatment. * Have a negative urine pregnancy test at screening. * Not to donate or freeze egg(s) during the course of this study or within 150 days after receiving their last dose of study drug. * Male patients even if surgically sterilized (i.e., status post-vasectomy) must agree to: * Use effective contraception during the entire study treatment period and through 150 days after the last dose of study drug. * Not to donate or freeze sperm during the course of this study or within 150 days after receiving their last dose of study drug. * Because there is an unknown but potential risk for adverse events in nursing infants secondary to treatment of the mother with atezolizumab and durvalumab, female participants who are breastfeeding must agree to discontinue breastfeeding. These potential risks may also apply to iadademstat * 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 participants

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Exclusion Criteria:

* Patients who receive maintenance ICI therapy prior to cycle 1, day 1 * Patients medicated with anti-depressants reported to have KDM1A/LSD1 inhibitory activity: Tranylcypromine or phenelzine * Patients who have not recovered from grade ≥2 adverse events (AEs) due to prior anti-cancer therapy with the exception of alopecia, vitiligo, and the laboratory values defined in the inclusion criteria. * Patients with grade ≥ 2 neuropathy will be evaluated on a case-by-case basis after consultation with the study physician * Patients who are receiving any other investigational agents or any other agent administered for the treatment of the patient's cancer within four half-lives or 4 weeks prior to registration, whichever is shorter * Treatment with systemic immunostimulatory agents (including, but not limited to, interferon \[IFN\]-α or interleukin \[IL\]-2) within 4 weeks or five half-lives of the drug (whichever is longer) prior to cycle 1, day 1 * Treatment with systemic immunosuppressive medications (including, but not limited to, prednisone, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor \[anti-TNF\] agents) within 2 weeks prior to registration or anticipation of need for systemic immunosuppressive medication during study treatment, with the following exceptions: * Patients who have received acute, low dose, systemic immunosuppressant medications or one-time pulse dose of systemic immunosuppressant medication (e.g., 48 hours of corticosteroids for a contrast allergy) are eligible after Principal Investigator confirmation has been obtained. * Patients who have received mineralocorticoids (e.g., fludrocortisone), corticosteroids for chronic obstructive pulmonary disease (COPD) or asthma, or low-dose corticosteroids for orthostatic hypotension or adrenocortical insufficiency are eligible * History of allergic reactions attributed to compounds of similar chemical or biologic composition to iadademstat, atezolizumab, or durvalumab. In particular, a history of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric antibodies, fusion proteins, or Chinese hamster ovary cell products or to any component of the atezolizumab formulation * Atezolizumab Concomitant Medication Considerations: Patients are not allowed to receive immunostimulatory agents, immunosuppressive medications, or herbal and natural remedies * Durvalumab Concomitant Medication Considerations: Patients are not allowed to receive immunosuppressive medications, EGFR TKIs, or herbal and natural remedies * Iadademstat Concomitant Medication Considerations: Patients are not allowed to receive prophylactic hematopoietic colony stimulating factors, any complementary or alternative medicine \[any of various systems of healing or treating disease (as non-prescription drugs, herbal medicine and homeopathy)\]. Use of these types of treatments must be terminated 1 week prior to registration * History of allogenic organ transplantation * Patients with active tuberculosis (TB) * Patients with uncontrolled intercurrent illness or any other significant condition(s) that would make participation in this protocol unreasonably hazardous * History of idiopathic pulmonary fibrosis, pneumonitis (including drug induced), organizing pneumonia (i.e., bronchiolitis obliterans, cryptogenic organizing pneumonia, etc.), or evidence of active pneumonitis on screening chest computed tomography (CT) scan. History of radiation pneumonitis in the radiation field (fibrosis) is permitted * Unstable angina, symptomatic or otherwise uncontrolled arrhythmia (does not include stable, lone atrial fibrillation), Fridericia's correction (QTcF) \> 480 ms based on screening electrocardiogram (ECG), myocardial infarction ≤ 3 months prior to registration, cerebrovascular accidents ≤ 3 months before registration. Patient has congestive heart failure New York Heart Association (NYHA) class 2, 3 or 4 or patients with a history of congestive

heart failure NYHA class 2, 3 or 4 in the past, unless a screening echocardiogram performed within 1 month prior to registration demonstrates a left ventricular ejection fraction that is ≥ 45% * History or risk of autoimmune disease, including, but not limited to, myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, antiphospholipid antibody syndrome, Wegener granulomatosis, Sjögren syndrome, Guillain-Barré syndrome, or multiple sclerosis, with the following exceptions: * Patients with a history of autoimmune-related hypothyroidism on a stable dose of thyroid replacement hormone may be eligible. * Patients with controlled Type 1 diabetes mellitus (HbA1c \< 8%) on a stable insulin regimen may be eligible. * Patients with eczema, psoriasis, lichen simplex chronicus, or vitiligo with dermatologic manifestations only (e.g., patients with psoriatic arthritis would be excluded) are permitted provided all of the following conditions are met: * Rash must cover less than 10% of body surface area (BSA). * Disease is well controlled at baseline and only requiring low potency topical steroids. * No acute exacerbations of underlying condition within the last 12 months (not requiring psoralen plus ultraviolet A radiation \[PUVA\], methotrexate, retinoids, biologic agents, oral calcineurin inhibitors; high potency or oral steroids) within the previous 12 months. * Any chronic skin condition that does not require systemic therapy. * Patients without active disease in the last 5 years may be included but only after consultation with the study physician. * Patients with celiac disease controlled by diet alone * Patients should not receive vaccines 30 days prior to registration. Patient is informed to not receive vaccines during treatment and through 30 days after the last dose of study treatment with the exception of seasonal influenza vaccines and vaccines intended to prevent SARS-CoV-2, pneumococcal infection and coronavirus disease 2019 (COVID-19). If a patient had received a live attenuated vaccine within 30 days of the first dose of trial treatment, eligibility should be discussed with the investigator * Patient has had major surgery within 4 weeks prior to registration * Patient has radiation therapy within 4 weeks prior to registration, excluding palliative and central nervous system (CNS) radiation * Manifestations of malabsorption due to prior gastrointestinal (GI) surgery, GI disease, or for an unknown reason that may alter the absorption of iadademstat. In addition, patients with enteric stomata are also excluded * Patients with history of clinically significant bleeding, specifically any history of intracranial hemorrhage / hemorrhagic cardiovascular accident (CVA), or patients with gastrointestinal bleeding within the 3 months prior to registration * Patients with known irreversible bleeding disorders or receiving antiplatelet therapy for other indications * Patients with uncontrolled disseminated intravascular coagulation * Patients who refuse or are unable to potentially receive blood products

Conditions & Interventions

Interventions:
BIOLOGICAL: Atezolizumab, PROCEDURE: Biopsy Procedure, PROCEDURE: Biospecimen Collection, PROCEDURE: Computed Tomography, BIOLOGICAL: Durvalumab, PROCEDURE: Echocardiography Test, DRUG: Iadademstat, PROCEDURE: Magnetic Resonance Imaging, PROCEDURE: Multigated Acquisition Scan
Conditions:
Extensive Stage Lung Small Cell Carcinoma, Stage IV Lung Cancer AJCC v8

More Information

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