Phase 1 Study of Shattuck Labs (SL)-172154 in Subjects With MDS or AML

Status: Recruiting

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

1. Subject has voluntarily agreed to participate by giving written informed consent in accordance with International Council for Harmonisation/Good Clinical Practice (ICH/GCP) guidelines and applicable local regulations. 2. Age ≥ 18 years. 3. For subjects with AML, confirmation of AML diagnosis by 2016 World Health Organization (WHO) criteria [Arber, 2016] classification, excluding acute promyelocytic leukemia (APL). 4. Subjects with MDS must have: 1. morphologically confirmed diagnosis of MDS by 2016 WHO criteria [Arber, 2016] with <20% blasts in bone marrow per bone marrow biopsy/aspirate or peripheral blood. 2. confirmation of intermediate, high or very high risk category by Revised International Prognostic Scoring System (IPSS-R) 5. Subjects with AML must have relapsed/refractory disease (>5% blasts by manual aspirate differential, flow cytometry, or immunohistochemistry) following at least 1 prior line of therapy but no more than 4 prior lines of therapy. 6. Subjects with relapsed/refractory disease (as defined in Inclusion criterion 5) following at least 1 prior line of therapy but no more than 4 prior lines of therapy for AML or MDS. 7. Subjects diagnosed with MDS must be previously untreated. Prior MDS therapy with lenalidomide or supportive care in the form of transfusions or growth factors is allowed. 8. All subjects must have documentation of at least one tumor protein 53 (TP53) gene mutation/deletion based on local test. 9. Subjects with previously untreated de novo AML or secondary AML with TP53 gene mutation or deletion and who are unlikely to benefit from standard intensive induction therapy or refuse intensive induction therapy at time of enrollment are eligible. All subjects must have documentation of at least one TP53 gene mutation/deletion based on local test. Subjects with secondary AML after MDS must not have received prior chemotherapy or no more than 2 cycles of prior hypomethylating agent for MDS. 10. Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0, 1, or 2 11. Laboratory values must meet the criteria outlined in the protocol. 12. Willing to provide consent for bone marrow aspirate samples for exploratory research at baseline and on-treatment per schedule described in the Schedule of Assessments. 13. For subjects with relapsed/refractory disease, recovery from prior anti-cancer treatments including surgery, radiotherapy, chemotherapy or any other anti-cancer therapy to baseline or ≤ Grade 1. 14. Females of childbearing potential (FCBP) must have a negative serum or urine pregnancy test within 72 hours of the first dose of study treatment. 15. Male subjects with female partners of childbearing potential must have azoospermia from a prior vasectomy or underlying medical condition or agree to use an acceptable method of contraception during treatment and for 30 days (which exceeds 5 half-lives) or for the duration required by local regulatory guidance, whichever is longer, after last dose of study treatment.

Exclusion Criteria:

1. Subject with relapsed or refractory disease has received treatment for AML or MDS with any of the following: 1. Chimeric antigen receptor (CAR)-T cell therapy 2. Prior treatment with anti-cluster of differentiation 47 (CD47) targeting agent or cluster of differentiation 40 (CD40) agonist within 28 days prior to 3. the first dose of study treatment. 4. Prior treatment with signal-regulatory protein alpha (SIRPα)-targeting antibody 5. Other experimental therapies for AML or MDS within 14 days or at least 5 half- lives (whichever is shorter) prior to the first dose of study treatment 2. Evidence of active central nervous system (CNS) involvement with leukemia 3. Subjects requiring agents other than hydroxyurea to control blast counts within 14 days prior to the first dose of study treatment. 4. Evidence of active bleeding or bleeding diathesis or major coagulopathy (including familial) 5. [Only for Cohorts including Venetoclax in the regimen] Subject has received strong and/or moderate cytochrome P450, family 3, subfamily A (CYP3A) inducers within 7 days prior to the first dose of study treatment. 6. Use of corticosteroids or other immunosuppressive medication, current or within 14 days of the first dose of study treatment 7. Receipt of live attenuated vaccine within 30 days of first dose of SL-172154 treatment, the exception is that vaccines for coronavirus disease 19 (COVID-19) are permitted. 8. Subject has active, uncontrolled infection (e.g, viral, bacterial, or fungal). Subjects are eligible if infection is controlled with antibiotics, antivirals and/or antifungals. 9. [Only for Cohorts including Venetoclax in the regimen] Subject has a malabsorption syndrome or other condition that precludes enteral route of administration. 10. Symptomatic peptic ulcer disease or gastritis, active diverticulitis, other serious gastrointestinal disease associated with diarrhea within 6 months of first dose of study treatment. 11. Clinically significant or uncontrolled cardiac disease including any of the following:

• Myocarditis

• Unstable angina within 6 months from D1 of study treatment

• Acute myocardial infarction within 6 months from D1 of study treatment

• Uncontrolled hypertension

• New York Heart Association (NYHA) Class III or IV congestive heart failure

• Clinically significant (symptomatic) cardiac arrhythmias (e.g., sustained ventricular tachycardia, second- or third- degree atrioventricular (AV) block without a pacemaker, circulatory collapse requiring vasopressor or inotropic support, or arrhythmia not stabilized on therapy) 12. Subject has chronic respiratory disease that requires continuous oxygen, or significant history of renal, neurologic, psychiatric, endocrinologic, metabolic, immunologic, hepatic, cardiovascular disease, or any other medical condition that in the opinion of the investigator would adversely affect his/her participation in the study. 13. Subjects who have had any major surgical procedure within 14 days of first dose of study treatment. 14. Subject is a woman who is pregnant or breast feeding or planning to become pregnant or breast feed while enrolled in this study. 15. Psychiatric illness/social circumstances that would limit compliance with study requirements and substantially increase the risk of adverse events (AEs) or compromised ability to provide written informed consent. 16. Presence of another malignancy that requires active therapy and that in the opinion of the investigator and Sponsor would interfere with the monitoring of disease assessments in this study. 17. Known hypersensitivity to any of the study medications including excipients of Azacitidine. 18. Has undergone solid organ transplantation. 19. Known or active human immunodeficiency virus (HIV) infection 20. Known or active infection with hepatitis B (positive for hepatitis B surface antigen [HBsAg]) or hepatitis C virus ([HCV]; if hepatitis C virus (HCV) antibody (Ab) test is positive check for HCV ribonucleic acid [RNA]).

Conditions & Interventions

Interventions:

Drug: SL-172154

Conditions:

Acute Myeloid Leukemia, Myelodysplastic Syndromes

More Information

Contact(s): Shattuck Clinical Trials - clinicaltrials@shattucklabs.com

Principal Investigator:

Phase: Phase 1

IRB Number:
System ID: NCT05275439

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