CLN-049 in Patients With Relapsed/Refractory Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS)

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 18 years and over
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

1. Aged ≥ 18 years of age.
2. Willing and able to give written informed consent and adhere to protocol requirements; written informed consent and any locally required authorization must be obtained from the patient prior to performing any protocol-related procedures, including screening evaluations, and serial samples of bone marrow and peripheral blood.
3. Patient has a confirmed diagnosis of recurrent or refractory AML or MDS.
4. Patient has received, and has progressed, recurred, or is intolerant of approved therapeutic options that are available, or declines treatment with these therapies.
5. White blood cell (WBC) count at the time of the first dose is < 20,000/uL (hydroxyurea is permitted according to standard institutional practice). Following first dose, WBC should be checked prior to subsequent CLN-049 administration and if WBC > 20,000/µL, CLN-049 treatment should be postponed (see Section 6.1 for further guidance).
6. Eastern Cooperative Oncology Group (ECOG) performance status is 0 to 2.
7. Toxicities related to prior study therapy should have resolved to Grade 1 or less according to criteria of NCI CTCAE v5.0, except for alopecia, lymphopenia, neutropenia, leukopenia, anemia, thrombocytopenia. Patients with chronic but stable toxicities may be allowed to enroll after agreement between the Investigator and Sponsor.
8. The patient's laboratory values meet the following criteria:

    1. Creatinine clearance (CrCl) as calculated by the Cockcroft-Gault formula (Appendix 1) must be ≥ 60 mL/min;
    2. Total bilirubin ≤ 1.5 × ULN. This does not apply for patients with confirmed Gilbert's Syndrome, hemolysis, or chronic blood transfusions, for whom total bilirubin must be less than 3.0 mg/dL with a conjugated bilirubin less than 0.5 mg/dL;
    3. AST and ALT ≤ 3.0 × ULN (unless attributed to leukemic involvement).

Exclusion Criteria:

1. Diagnosis of acute promyelocytic leukemia (APL)
2. Active central nervous system (CNS) leukemia. For patients with a history of CNS leukemia, a lumbar puncture should be performed during screening to exclude the presence of active CNS involvement.
3. Isolated extramedullary relapse
4. Prior organ allograft
5. Allogeneic hematopoietic transplantation within six months of treatment, or with clinical or laboratory evidence of GVHD, or requiring ongoing treatment with immune suppression within 2 months of the first dose of CLN-049.
6. Treatment with any of the following:

    1. Radiation therapy (XRT) within 28 days of the first dose of CLN049, or craniospinal XRT within 8 weeks of the first dose of CLN-049, or history of total body irradiation (TBI).
    2. Prior immunotherapy with checkpoint inhibitors ≤ 42 days prior to the first dose of CLN-049.
    3. Prior history of chimeric antigen receptor (CAR-T) cell therapy or other modified T cell therapy.
    4. Anti-leukemic therapy except hydroxyurea for cytoreduction, and intrathecal chemotherapy ≤ 14 days or 5 half-lives, whichever is shorter, prior to the first dose of CLN-049.
    5. Short-acting hematopoietic growth factors ≤ 7 days prior to the first dose of CLN-049
    6. Long-acting growth factors ≤ 14 days prior to the first dose of CLN-049.
    7. Systemic glucocorticoid therapy (except equivalent of < 10 mg prednisone daily) or other immune-suppressive drugs ≤ 14 days prior to the first dose of CLN-049 (see separate guidelines for patients who are post allogeneic hematopoietic transplantation). The transient use of corticosteroids for transfusion premedication or the treatment of infusion or transfusion reactions will not be considered for this criterion. Topical corticosteroids and steroid eye drops are allowed, and will not exclude the patient from eligibility.
    8. Prior treatment with a FLT3-directed bispecific molecule, or a FLT3-targeted antibody.
7. Currently participating/previously participated in an interventional study and received an investigational drug within 14 days (or five half-lives, whichever is longer) prior to the first dose of CLN-049.
8. Patients with concomitant second malignancies requiring active treatment in the past 12 months, or if additional therapy is required or anticipated during study participation.
9. Patients with any active autoimmune disease or a history of known or suspected autoimmune disease, or history of a syndrome that requires systemic corticosteroids or immunosuppressive medications, except for patients with vitiligo, psoriasis (in consultation with the Sponsor), resolved childhood asthma/atopy or autoimmune thyroid disorders on stable thyroid hormone supplementation.
10. A serious uncontrolled medical disorder that would impair the ability of the patient to receive protocol therapy or whose control may be jeopardized by the complications of this therapy.

11. Any concurrent condition, therapy, or laboratory abnormality that, in the opinion of the investigator, might compromise patient safety or interfere with the evaluation of the safety of the drug.
12. Active uncontrolled infection within seven days of first dose of CLN-049. Prophylactic use of systemic antiviral, antibacterial, or antifungal agents for treatment of chronic, controlled infection or as prophylaxis is permitted.
13. Has a history of, or a positive test for Human Immunodeficiency Virus (HIV) 1/2 or primary immunodeficiency disease such as HIV.
14. Known history of hepatitis B (with positive testing for either hepatitis B surface antigen [HBsAg] or hepatitis B core Ab), hepatitis C (HCV) infection (with positive testing for HCV antibody and/or HCV ribonucleic acid [RNA] in serum), or acute hepatitis A (with positive testing for hepatitis A IgM). Note: patients with chronic HCV with undetectable viral load defined by sustained virologic response 24 weeks (SVR24) after completion of anti-hepatitis C treatment will be eligible. Patients with hepatitis B surface antigen [HBsAg] or hepatitis B core Ab with negative viral load will be eligible.
15. Active severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection including history of positive SARS-CoV-2 testing without subsequent documentation of negative test results, patients with results that are pending but not yet known, or patients with suspected active infection based on clinical features
16. History of the following events in conjunction with prior treatment with immunotherapy: Grade 3 or greater neurotoxicity, ocular toxicity, pneumonitis, myocarditis, or colitis; liver dysfunction meeting the laboratory criteria for Hy's Law.
17. Live virus vaccines within 28 days of the first dose of CLN-049, during treatment, and until the end of last dose of CLN-049.
18. Woman of child-bearing potential (WOCBP) who is pregnant or breast-feeding, plans to become pregnant within 120 days of last study drug administration, or declines to use an acceptable method to prevent pregnancy during study treatment and for 120 days after the last dose of study drug administration.
19. Male patient who plans to father a child or donate sperm within 120 days of last study drug administration, or who has a partner who is a WOCBP, and declines to use acceptable method to prevent pregnancy during study treatment and for 120 days after the last dose of study drug administration.
20. QT interval corrected for heart rate using Fridericia's formula (QTcF) of ≥ 480 milliseconds.
21. Patient has history of drug-related anaphylactic reactions to any components of CLN-049. History of Grade 4 anaphylactic reaction to any bispecific molecule or monoclonal antibody therapy.
22. Known history of prior human anti-human antibody response. Patients will not be screened for human anti-human antibody prior to study participation.
23. Known active alcohol or drug abuse.
24. Patients who are incapacitated or involuntarily incarcerated.

Conditions & Interventions

Interventions:
DRUG: CLN-049
Conditions:
Relapsed/Refractory Acute Myeloid Leukemia (AML), Myelodysplastic Syndrome (MDS)

More Information

Description:
CLN-049-001 is a Phase 1, open-label, multicenter, first-in-human trial of CLN-049 in patients with Relapsed/Refractory Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS)

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