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A Phase 1, Open-Label, Dose-Escalation and Dose-Expansion Study of CLN-049 for the Treatment of Acute Myeloid Leukemia Patients With Measurable Residual Disease

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BACKGROUND

- Substantial unmet medical needs remain for patients with acute myeloid leukemia (AML), whom often have measurable residual disease (MRD) at the end of induction therapy, which can lead to disease recurrence[1]
- Emerging approaches to improve outcomes include novel targeted therapies and immunotherapies to eradicate MRD in patients with AML who are at high risk of relapse
- FMS-like tyrosine kinase 3 (FLT3) is expressed on AML cells in more than 80% of patients and plays a key role in promoting leukemic cell proliferation and survival[2,3]

CLN-049: A NOVEL FLT3 AND CD3 BISPECIFIC ANTIBODY

- CLN-049 is a humanized bispecific antibody with dual binding specificities for FLT3 and CD3 on a human immunoglobulin G1 backbone with a silenced fragment crystallizable domain
- CLN-049 effectively redirects CD3+ T cells to kill FLT3-expressing AML cells within the blood and bone marrow to exert antileukemic effect
- CLN-049 is capable of binding to both wild-type or mutant FLT3

KEY INCLUSION AND EXCLUSION CRITERIA

Inclusion	Exclusion

• Age ≥18 years
• Patients with AML defined by the following 3 criteria:
  ○ In complete morphologic remission (CR, CRh, or CRi in accordance with European LeukemiaNet 2022 recommendations)[4]
  ○ Persisting MRD, defined as MRD detected in 2 consecutive samples
  ○ Have exhausted or are ineligible to receive available treatment alternatives, or are expected to receive alternative therapy (eg, allo-HSCT) at a later date
• ECOG performance status: 0 or 1
	• Allo-HSCT within 60 days of treatment
	• Prior treatment with:
	  ○ CAR-T therapy or other modified T-cell therapy
	  ○ FLT3-directed bispecific molecule or a FLT3-targeted antibody

allo-HSCT, allogeneic hematopoietic stem cell transplantation; CAR-T, chimeric antigen receptor T cell; CD3, cluster of differentiation 3; CR, complete remission; CRh, complete remission with partial hematologic recovery; CRi, complete remission with incomplete hematologic recovery; ECOG, Eastern Cooperative Oncology Group; MRD, measurable residual disease

KEY STUDY OBJECTIVES AND ENDPOINTS

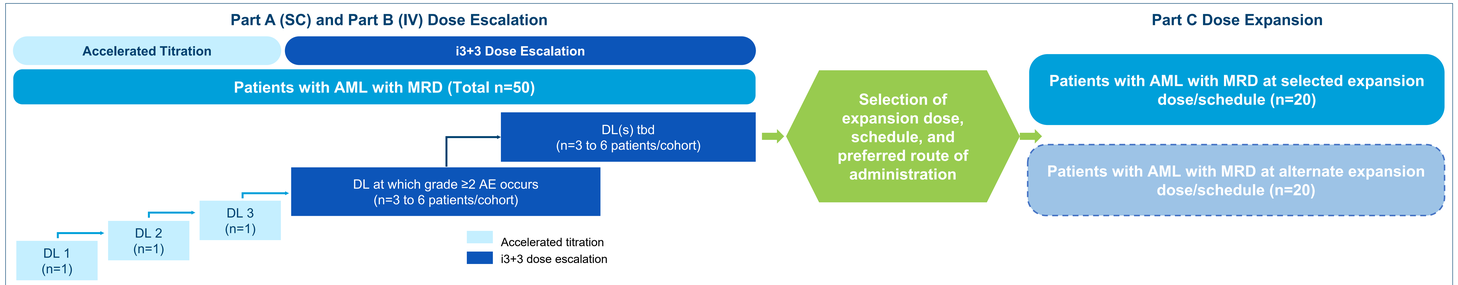
		Study objectives	Endpoints
Part A: Dose escalation	Primary	To characterize the safety and tolerability of CLN-049 in patients with MRD-positive AML	• Incidence and severity of AEs/AESIs/SAEs • Incidence of dose interruptions and delays • DLTs
	Secondary	To assess the preliminary antileukemic activity of CLN-049	• Proportion of patients achieving MRD negativity • Time to MRD negativity • Duration of MRD negativity • Time to disease progression (MRD relapse or morphologic relapse) • TTNT • PFS • OS
		To assess the PK of CLN-049	• Serum concentrations of CLN-049 • Estimated PK parameters as the data allow
		To evaluate the immunogenicity of CLN-049 and assess potential impact on drug exposure	• Incidence of ADAs to CLN-049
Part B: Dose expansion	Primary	To assess the preliminary antileukemic activity of CLN-049	• Proportion of patients achieving MRD negativity • Time to MRD negativity • Duration of MRD negativity • Time to disease progression • TTNT • PFS • OS
		To further assess the safety and tolerability of CLN-049 in patients with MRD-positive AML	• Incidence and severity of AEs/AESIs/SAEs • Incidence of dose interruptions and delays
	Secondary	To further characterize select PK parameters associated with CLN-049	• Serum concentrations of CLN-049 • Estimated PK parameters as the data allow
		To evaluate the immunogenicity of CLN-049 and assess potential impact on drug exposure	• Incidence of ADAs to CLN-049

ADA, antidrug antibody; AE, adverse event; AESI, adverse event of special interest; DLT, dose-limiting toxicity; MRD, measurable residual disease; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; SAE, serious adverse event; TTNT, time to next antileukemia therapy

CLN-049-002 STUDY DESIGN (EU CT: 2023-506572-27-00)

- Approximately 70 patients (50 in dose escalation and 20 in dose expansion) will be enrolled at 12 sites, including both community and academic centers

Figure 1: CLN-049-002: phase 1, open-label, multicenter, dose-escalation and dose-expansion study



Dose Escalation commencing with accelerated titration in single-patient cohorts followed by an i3+3 dose-escalation design to explore both SC and IV routes of administration to identify the MTD, or MAD if no MTD is defined

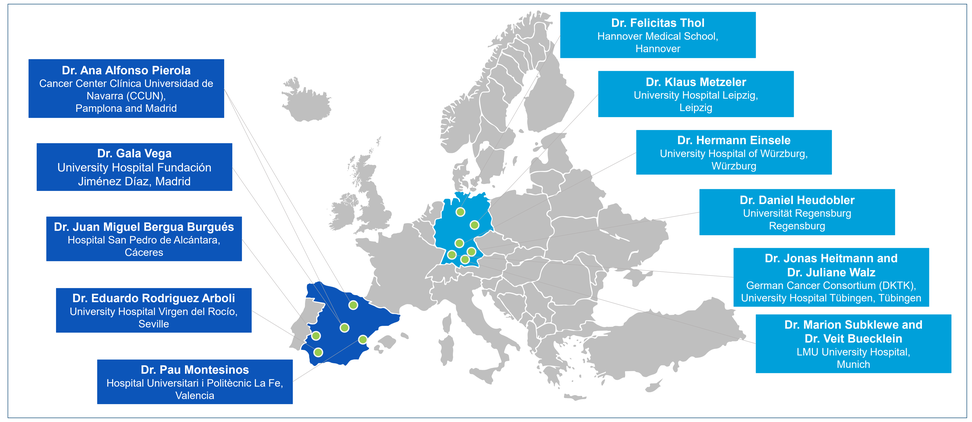
Dose Expansion will further characterize the safety and preliminary efficacy of CLN-049 in this patient population at the dose, schedule, and preferred route of administration determined in the dose-escalation phase to allow determination of a RP2D

AE, adverse event; DL, dose level; i3+3, interval 3+3; IV, intravenous; MAD, maximum administered dose; MRD, measurable residual disease; MTD, maximum tolerated dose; RP2D, recommended phase 2 dose; SC, subcutaneous; tbd, to be determined

- CLN-049 will be administered every 7 days in 21-day cycles until morphologic relapse, unacceptable toxicity, proceeding to alternative treatment (eg, allogeneic hematopoietic stem cell transplantation [allo-HSCT]), or a maximum of 12 weeks of treatment
- The initial administration of CLN-049, including potential step-up doses and the first target dose, will be administered on an inpatient basis
- Subsequent doses may be given in the outpatient setting
- Safety, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary efficacy assessments will guide dose selection and schedule for further evaluation

STUDY SITES

Figure 2: The study is currently enrolling patients in Germany and Spain



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