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cAMeLot-2: A Phase 3 Randomized, Double-Blind, Placebo-Controlled Study of Bleximenib, Venetoclax, and Azacitidine for the Treatment of Participants With Newly Diagnosed Acute Myeloid Leukemia Harboring *KMT2A* Rearrangements or *NPM1* Mutations Who Are Ineligible for Intensive Chemotherapy

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Key Takeaway

cAMeLot-2 is a currently enrolling phase 3, randomized, double-blind, placebo-controlled, global multicenter study evaluating the efficacy and safety of bleximenib with venetoclax and azacitidine in adults with ND AML harboring *KMT2A* rearrangements or *NPM1* mutations who are ineligible for IC

Registration Information

This study is registered with EUclinicaltrials.eu (EU CT number: 2024-520154-3) and ClinicalTrials.gov (NCT06852222)

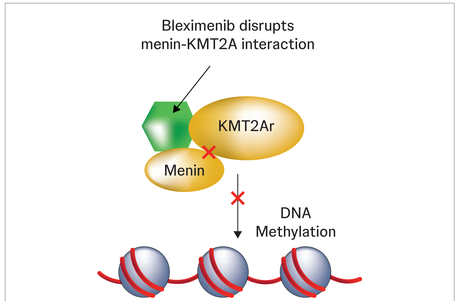
Background

- Newly diagnosed (ND) acute myeloid leukemia (AML) is a genetically heterogeneous disease with a 5-year overall survival rate of ~30% for all patients[1,2] and <10% for those aged ≥65 years and ineligible for intensive chemotherapy (IC)[3]
- *KMT2A* rearrangements (*KMT2Ar*) or *NPM1* mutations (*NPM1m*) in patients with AML who are aged ≥65 years are associated with poor treatment outcomes[4,5]
- Older patients or those with comorbidities have limited tolerance to IC and are typically treated with hypomethylating agents, such as azacitidine (AZA) plus venetoclax (VEN)[4]
- Bleximenib is a potent menin inhibitor with activity in *KMT2Ar* and *NPM1m* AML (**Figure 1**).[6] No menin inhibitors are currently approved for patients with ND *KMT2Ar* or *NPM1m* AML ineligible for IC
- In the phase 1b ALE1002 study (NCT05453903), high rates of response were observed with bleximenib at 100 mg twice daily (BID; the recommended phase 2 dose [RP2D]) in combination with VEN + AZA in participants with ND *KMT2Ar* or *NPM1m* AML[7]
  - The safety profile of bleximenib in combination with VEN + AZA was consistent with the VEN + AZA backbone, with low rates of differentiation syndrome events and no QTc prolongation signal identified
  - No drug-drug interactions with VEN + AZA were observed

Objective

- To evaluate efficacy and safety of bleximenib with VEN + AZA in adults with ND *KMT2Ar* or *NPM1m* AML who are ineligible for IC

Figure 1: Mechanism of action of bleximenib

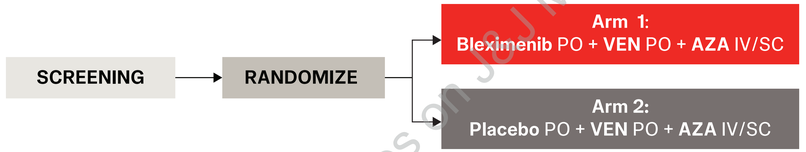


Methods

Study design

- cAMeLot-2 (EU CT number 2024-520154-38; NCT06852222) is a phase 3, randomized, double-blind, placebo-controlled, global multicenter study
- 600 participants will be randomly assigned to bleximenib 100 mg BID or placebo, both in combination with VEN + AZA. Treatment will be administered on a 28-day cycle and continued until progression or unacceptable toxicity (**Figure 2**)

Figure 2: cAMeLot-2 study design



Endpoints

Primary endpoints	
Percentage of participants who achieve complete remission (CR)	CR is defined as bone marrow blasts <5%, absence of circulating blasts, absence of extramedullary disease, absolute neutrophil count ≥1 x 10^9/L, and platelet count ≥100 x 10^9/L
Overall survival	Defined as the duration of time from the date of randomization to death due to any cause
Secondary endpoints	
Duration of CR **Time to CR** **Rate of CR without measurable residual disease** **Percentage of participants who achieved transfusion independence**	**Percentage of participants with allo-HSCT** **Number of participants with adverse events** **Number of participants with abnormalities in clinical laboratory parameters** **Serum concentration of bleximenib**

Eligibility criteria

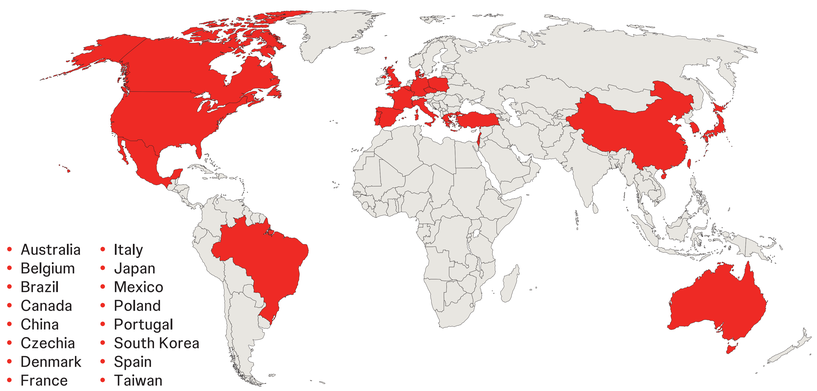
Key inclusion criteria	Key exclusion criteria
• Age ≥18 years • ND *KMT2Ar* or *NPM1m* AML[a] • Ineligible for IC[b] • Adequate hepatic and renal function	• Diagnosis of acute promyelocytic leukemia (APL) • Known active leukemic involvement of the CNS • Active infectious hepatitis • Significant cardiac disorder ≤6 months prior to randomization

[a]≥10% bone marrow blasts per 2022 International Consensus Classification criteria.
[b]Based on: [a] ≥75 years and ineligible per physician's discretion, Eastern Cooperative Oncology Group performance status (ECOG PS) of 0–2, or [b] ≥18 to <75 years with ≥1 of the following comorbidities: ECOG PS of 2; severe cardiac or pulmonary disorder; renal impairment; comorbidity that, in the investigator's opinion, makes the participant unsuitable for IC.

Study enrollment

- Enrollment is ongoing globally (**Figure 3**)

Figure 3: Countries currently enrolling in cAMeLot-2 study



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- United States

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Acknowledgments

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Abbreviations

allo-HSCT, allogeneic hematopoietic stem cell transplant; AML, acute myeloid leukemia; APL, acute promyelocytic leukemia; AZA, azacitidine; BID, twice daily; CNS, central nervous system; CR, complete remission; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, intensive chemotherapy; IV, intravenous; *KMT2A*, lysine methyltransferase 2A gene; *KMT2Ar*, *KMT2A* rearranged; ND, newly diagnosed; *NPM1*, nucleophosmin 1 gene; *NPM1m*, *NPM1* mutated; PO, orally; QTc, corrected QT interval; RP2D, recommended phase 2 dose; SC, subcutaneous; VEN, venetoclax.

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Myeloid Malignancies

Presented by Elias Jabbour at the American Society of Hematology (ASH) Annual Meeting; December 6–9, 2025; Orlando, Florida