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VYSION (VYxeoS® liposomal Italian Observational study iN the real practice): Study Design and Baseline Characteristics

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Background

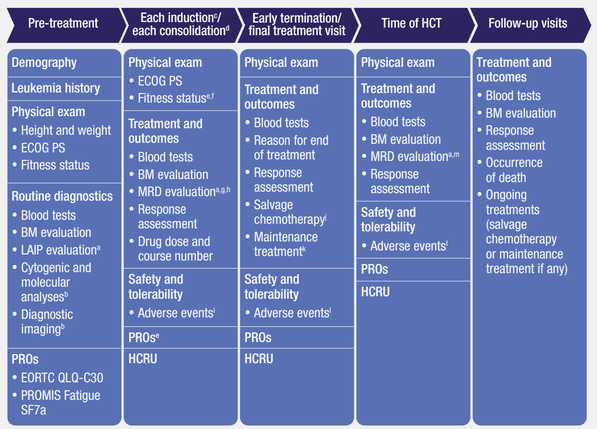
- CPX-351, a dual-drug liposomal encapsulation of daunorubicin and cytarabine in a synergistic 1:5 molar ratio, is approved for newly diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) in adult and pediatric (aged ⩾1 year) patients in the United States and adults in Europe[1-4]
- In the pivotal phase 3 trial (ClinicalTrials.gov identifier: NCT01696084), CPX-351 demonstrated significantly improved overall survival and remission rates vs conventional 7+3 chemotherapy, and a comparable safety profile in older adults aged 60-75 years with newly diagnosed, high-risk or secondary AML[1]
  - Survival benefit with CPX-351 vs 7+3 was maintained after 5 years of follow-up[5]
- While the pivotal trial established the efficacy and safety of CPX-351, it was conducted under controlled conditions with stringent eligibility criteria, inherent to the study design of clinical trials, limiting the generalizability of these results
- Several retrospective studies of CPX-351 have since been conducted across different countries in broader patient populations treated in real-life healthcare settings, complementing the trial findings and supporting clinical decision-making[6]
- However, no prospective studies of CPX-351 have been conducted, with limited insights into quality of life and the lack of standardized assessment of measurable residual disease (MRD),[7] highlighting the need for such studies to further complement prospective clinical trial data

Objective

- VYSION (VYxeoS® liposomal Italian Observational study iN the real practice; ClinicalTrials.gov identifier: NCT06143839) is the first prospective, single-arm, non-experimental, observational study of CPX-351 designed to evaluate the effectiveness and safety of CPX-351 in adults with t-AML or AML-MRC receiving CPX-351 as part of their normal clinical care
- Here, we describe the study design and summarize the baseline characteristics of enrolled patients

Study Design

Figure 1. Study Design and Patient Evaluations



[a]MFC-LAIP/MFC-MRD performed at a local level, validation performed in the centralized laboratory at end of study; [b]If performed following normal clinical practice; [c]Induction 2 may be administered in patients who do not show disease progression or unacceptable toxicity; [d]Up to 2 consolidation courses; [e]Optional assessment at induction 1, to be performed in case of >-20 days between pre-treatment evaluation and day 1 of Induction 1; [f]Optional evaluation at induction 2 and each consolidation; [g]If performed in the normal clinical practice. Assessment after Induction 1 or 2 will be collected for primary objective evaluation for patients not proceeding to consolidation courses, as end of treatment; [h]Assessment after consolidation 1 will be collected as end of consolidation/treatment for primary objective evaluation for patients not proceeding to consolidation 2. Assessment after consolidation 2 will be collected as end of consolidation/treatment for primary objective evaluation for patients receiving 2 consolidation courses; [i]Adverse events will be collected from day 1 of infusion of cycle 1 to 30 days after the last day of infusion of the last treatment cycle of CPX-351; [j]In case of early termination, if the patient is moved to second-line treatment; [k]In case of final treatment visit, if the patient is initiated to maintenance treatment; [l]If HCT/early termination/final treatment visit is performed by 30 days after the last infusion of CPX-351 last course; [m]Assessment at the time of HCT will be collected for secondary objective evaluation if available in the normal clinical practice.

BM, bone marrow; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30; HCRU, healthcare resource utilization; HCT, hematopoietic cell transplantation; LAIP, leukemia-associated immunophenotypes; MFC-LAIP; multiparametric flow cytometry leukemia-associated immunophenotypes; MFC-MRD, multiparametric flow cytometry measurable residual disease; MRD, measurable residual disease; PRO, patient-reported outcome; PROMIS, Patient-Reported Outcomes Measurement Information System®.

- This study is being conducted at 24 hematology sites, experienced in the treatment of t-AML and AML-MRC
- The study will collect patients' data via the electronic Case Report Form following the observational nature of the study, if performed in the normal clinical practice and available at each site for registration
- All enrolled patients will be observed until the last enrolled patient still alive has been followed for 12 months

Table 1. Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
• Patients newly diagnosed with t-AML or AML-MRC (following 2016 WHO classification) • Aged ⩾18 years old • Patients considered eligible for intensive chemotherapy in the opinion of the treating physician (regardless of eligibility to HCT) • Patients who will initiate the treatment with CPX-351 after the ICF signature. The decision to prescribe CPX-351 treatment must have been made prior to and regardless of the enrollment of the patient in the study • Cardiac ejection fraction ⩾50% by echocardiography or MUGA • Patients with second malignancies in remission may be eligible if there is clinical evidence of disease stability for a period of >6 months off cytotoxic chemotherapy, documented by imaging, tumor marker studies, etc., at screening. Patients maintained on long-term non-chemotherapy treatment, e.g., hormonal therapy, are eligible • Ability to understand and voluntarily give informed consent. As necessary, consent may be obtained from the patient's legally authorized representative on the patient's behalf in accordance with applicable legislation	• Prior treatment intended for induction therapy of AML; only hydroxyurea is permitted for control of blood counts • Patients with prior cumulative anthracycline exposure of >368 mg/m^2 daunorubicin (or equivalent) • Clinical evidence of active CNS leukemia • Patients with active (uncontrolled, metastatic) second malignancies • Patients simultaneously participating in another study which includes an investigational drug

AML, acute myeloid leukemia; AML-MRC, acute myeloid leukemia with myelodysplasia-related changes; CNS, central nervous system; HCT, hematopoietic cell transplantation; ICF, Informed Consent Form; MUGA, Multiple Gated Acquisition scan; t-AML, therapy-related acute myeloid leukemia; WHO, World Health Organization.

- The decision to prescribe CPX-351 treatment must have been made prior to and regardless of enrollment in the study
- Eligible patients are to have been treated with CPX-351 according to the current European Summary of Product Characteristics[3]
  - Induction: 1 to 2 courses of CPX-351 100 units/m^2 (daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2) as a 90-minute infusion on days 1, 3, and 5 (days 1 and 3 only for the second induction)
  - Consolidation: Up to 2 courses of CPX-351 65 units/m^2 (daunorubicin 29 mg/m^2 and cytarabine 65 mg/m^2) as a 90-minute infusion on days 1 and 3

Table 2. Study Endpoints

Primary Endpoint	Secondary Endpoints	Exploratory Endpoints
• Percentage of patients who achieve CR/CRi/CRh without MRD at the end of treatment,[a] assessed per the 2022 ELN response criteria	• Overall response rate (CR+CRi+CRh) after induction • CR/CRi/CRh rate without MRD post-induction and pre-transplantation (if applicable) • OS from CPX-351 treatment initiation date • HCT rate • OS landmarked from HCT date • Safety, including AEs of special interest and serious AEs • Patient fitness status (per Ferrara criteria) before HCT and at the final treatment visit for patients ineligible for HCT	• Rate of patients with complete genetic diagnosis at baseline, based on 2022 ELN guidelines • Rate of outpatient management during induction and/or consolidation • Change in PROs during treatment including at the end of induction phase, at the end of consolidation phase, and before HCT: Fatigue and global health status assessment through the Patient-Reported Outcomes Measurement Information System Fatigue SF7a, and quality of life through EORTC QLQ-C30 • Measurement of hospital and ICU stays, anti-infective use, transfusions, and white blood cell CSF use • Identification of prognostic factors that influence CR/CRi/CRh MRD– and OS in patients treated with CPX-351

[a]End of treatment was defined as last response evaluation after the last treatment cycle.

AE, adverse event; CR, complete remission; CRh, complete remission with partial hematologic recovery; CRi, complete remission with incomplete platelet or neutrophil recovery; CSF, colony-stimulating factor; ELN, European LeukemiaNet; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30; HCT, hematopoietic cell transplantation; ICU, intensive care unit; MRD, measurable residual disease; MRD–, measurable residual disease negativity; OS, overall survival; PRO, patient-reported outcome.

- Bone marrow samples will be assessed locally for MRD via multiparameter flow cytometry (MFC), with MRD negativity defined as <10^{-3} per the 2021 European LeukemiaNet guidelines[8]

Study Update

- The study observation closed in October 2025, with the analysis planned in 2026
- As the first prospective observational study of CPX-351, VYSION directly collects data during patient treatment, enhancing the clinical significance of the findings
- Furthermore, this prospective design uniquely enables the collection of quality of life data and the standardized assessment of CPX-351's impact on MRD via MFC at key time points
- VYSION has the potential to provide valuable insights into effectiveness and safety of CPX-351 in routine clinical practice

Table 3. Baseline Patient and Disease Characteristics

	Overall (N=106)
Age	
Median (Q1, Q3), years	68 (61, 71)
<60 years, n (%)	21 (20)
⩾60 years, n (%)	85 (80)
Sex, n (%)	
Male	62 (58)
Female	44 (42)
Race, n (%)	
White	101 (95)
African	1 (1)
Asian	2 (2)
Unknown	2 (2)
Ethnicity, n (%)	
Hispanic or Latino	14 (13)
Not Hispanic or Latino	92 (87)
ECOG PS,[a] n (%)	
0	70 (69)
1	31 (31)
Missing, n	5
Disease classification, n (%)	
t-AML	22 (21)
AML-MRC	84 (79)
History of MDS or MDS/MPN[b]	34 (40)
MDS-related cytogenic abnormality[b]	29 (35)
Multilineage dysplasia[b]	35 (42)
Prior treatment with hypomethylating agent,[c] n (%)	11 (58)
Molecular abnormalities, n (%)	
FLT3-ITD mutations[d,e]	6 (6)
TP53 mutations[d]	20 (21)
Myelodysplasia-related gene mutations[d]	34 (35)
Abnormal karyotype,[f] n (%)	59 (57)
2022 European LeukemiaNet Risk Category[g]	
Favorable	7 (7)
Intermediate	29 (28)
Adverse	68 (65)
Number of ongoing comorbidities	
0	16 (15)
1	27 (25)
2	19 (18)
⩾3	44 (42)

Percentages are calculated based on the available dataset, excluding missing values.

[a]Percentages were calculated out of total number of patients with non-missing data; [b]Multiple choices are allowed therefore some patients fit into more than one category of AML-MRC; [c]Out of 19 patients with a history of MDS or MDS/MPN and available data on prior therapy; [d]Out of 97 patients with available data screened for gene mutations; [e]There were no patients with *FLT3-TKD* mutations; [f]Out of 103 patients with available cytogenic data; [g]2 patients had missing data.

AML-MRC, acute myeloid leukemia with myelodysplasia-related changes; ECOG PS, Eastern Cooperative Oncology Group performance status; *FLT3-ITD*, FMS-like tyrosine kinase 3 internal tandem duplication; *FLT3-TKD*, FMS-like tyrosine kinase 3 tyrosine kinase domain; MDS, myelodysplasia; MPN, myeloproliferative neoplasms; Q1, quartile 1; Q3, quartile 3; t-AML, therapy-related acute myeloid leukemia; *TP53*, tumor protein p53.

- At data cutoff (May 16, 2025), VYSION has enrolled 112 patients and 106 were included in this analysis of baseline patient and disease characteristics
- Of patients assessed for transplantation eligibility, 96% (75/78) were eligible
- Overall, 94% (100/106) of patients were considered eligible for intensive chemotherapy in the investigator's opinion
- Ferrara criteria assessment for fitness evaluation was performed in 83% (88/106) of patients
- In patients assessed by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 with available data, mean global health status was 54 (standard deviation [SD]: 22.9; n=99) and mean physical functioning score was 78 (SD: 20.1; n=101)

References: 1. Lancet JE, et al. *J Clin Oncol.* 2018;36(26):2684-2692. **2.** VYXEOS® (daunorubicin and cytarabine) liposome for injection, for intravenous use [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; 2022. **3.** Vyxeos liposomal (44 mg/100 mg powder for concentrate for solution for infusion) summary of product characteristics. European Medicines Agency: Jazz Pharmaceuticals Ireland, Ltd.; 2024. **4.** Vyxeos liposomal (44 mg/100 mg powder for concentrate for solution for infusion) summary of product characteristics. Electronic Medicines Compendium: Jazz Pharmaceuticals UK, Ltd.; 2025. **5.** Lancet JE, et al. *Lancet Haematol.* 2021;8(7):e481-e491. **6.** Lemoli RM, et al. *Crit Rev Oncol Hematol.* 2023;185:103984. **7.** Cloos J, et al. *Hematology Am Soc Hematol Educ Program.* 2019;2019(1):617-625. **8.** Heuser M, et al. *Blood.* 2021;138(26):2753-2767.

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