Early Cytarabine Escalation Does Not Improve Short-Term Outcomes Compared With Hydroxyurea-Only Cytoreduction in Hyperleukocytic Acute Myeloid Leukemia

A Real-World Propensity-Matched Analysis of 5,846 Patients

Bibek Shrestha MD[1], Marina Khan MD[1], Milan Regmi MD[2], Akshay Aluri MD[1], Drew Oostra MD[1], Divya Vijendra MD[1], Shahab Uddin MD[1], Danae Hamouda MD[1]

[1]University of Toledo Medical Center, Toledo, Ohio, USA [2]Southeast Health Medical Center, Dothan, Alabama, USA

Presenting author underlined

SOHO 2026

Fourteenth Annual Meeting
Society of Hematologic Oncology

September 9–12, 2026 · Houston, Texas

Abstract 1478

1 Background

- Hyperleukocytosis is a hematologic emergency in newly diagnosed AML, driven by leukostasis, tumor lysis and coagulopathy.
- Early death in the first days after presentation remains a major contributor to overall AML mortality.
- Urgent cytoreduction options include hydroxyurea, early cytarabine-based chemotherapy and leukapheresis.
- Practice varies widely and no randomized data compare early cytarabine escalation with hydroxyurea-only cytoreduction.

2 Objective

Does early cytarabine-based cytoreduction improve short-term mortality or complications versus hydroxyurea alone?

3 Methods

Design	Retrospective cohort study in the TriNetX global health research network — multicenter international EHR data.
Population	Adults, newly diagnosed non-APL AML with hyperleukocytosis.
Exposure (≤ 72 h)	Cytarabine-based therapy ± hydroxyurea versus hydroxyurea alone; leukapheresis excluded.
Matching	1:1 propensity score matching on demographics, comorbidities, baseline labs, WBC category and illness severity.
Outcomes	Primary: 30-day all-cause mortality. Secondary: 7- and 14-day mortality, leukostasis, TLS, DIC, AKI and dialysis.

4 Study Population

TriNetX global health research network

Adults, newly diagnosed non-APL AML with hyperleukocytosis

Cytoreduction started ≤ 72 h · leukapheresis excluded

1:1 propensity score matching

Cytarabine-based ± hydroxyurea	Hydroxyurea only
2,923 matched	2,923 matched

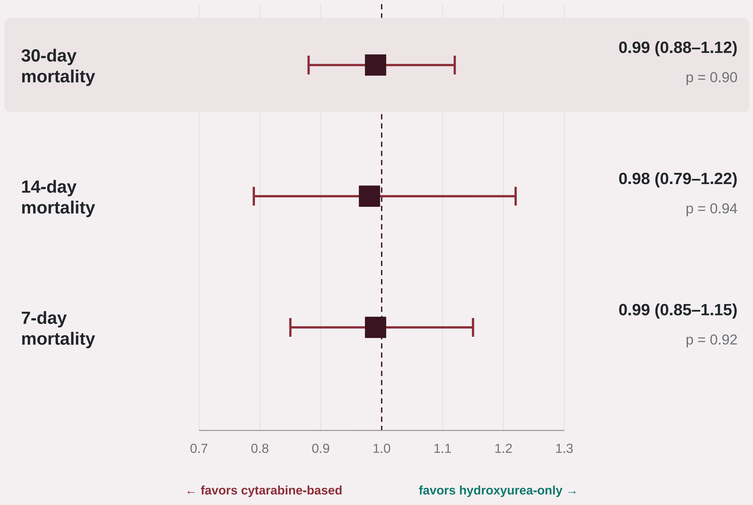
5,846
Propensity-matched patients analysed

≤ 72 h
Window defining early cytoreduction

HR 0.99
30-day mortality
95% CI 0.88–1.12 · p = 0.90

5 Early Mortality Outcomes

Cytarabine-based ± hydroxyurea versus hydroxyurea only — hazard ratios (95% CI) for all-cause mortality



No significant difference in mortality at any time point

6 Secondary Outcomes

Leukostasis-related complications	no difference
Tumor lysis syndrome	no difference
Disseminated intravascular coagulation	no difference
Acute kidney injury	no difference
Dialysis requirement	no difference

7 Sensitivity Analyses

WBC ≥ 100,000/µL	Consistent — no significant difference
WBC ≥ 150,000/µL	Consistent — no significant difference

Leukapheresis-treated patients were excluded from the primary analysis.

8 Conclusions

- Among 5,846 propensity-matched adults with hyperleukocytic AML, early cytarabine-based cytoreduction was not associated with lower all-cause mortality at 7, 14 or 30 days than hydroxyurea-only cytoreduction.
- No differences were observed in leukostasis-related complications, tumor lysis syndrome, DIC, acute kidney injury or dialysis requirement.
- Findings were consistent in the highest-risk subgroups (WBC ≥ 100,000/µL and ≥ 150,000/µL).

Escalation to early cytarabine-based therapy may not confer measurable early clinical benefit over supportive cytoreduction alone in routine practice.

9 Clinical Implications

- Hydroxyurea-only cytoreduction appears to be a reasonable initial approach while definitive, risk-adapted therapy is planned.
- Decisions to escalate early to cytarabine should weigh toxicity, organ function and readiness for induction rather than an assumed early survival benefit.
- Results address the first 30 days only; they do not speak to remission rates, long-term survival or the role of leukapheresis.
- Prospective, risk-adapted trials are needed to define optimal early cytoreduction in hyperleukocytic AML.

10 Limitations

- Retrospective EHR-based design; residual confounding and confounding by indication cannot be excluded.
- Exposure defined by coded medication timing — dose, intensity and sequencing were not captured.
- Cytogenetic and molecular risk, performance status and blast percentage were unavailable for matching.
- Outcomes were limited to 30 days and leukapheresis-treated patients were excluded.