REAL-WORLD COMPARISON OF HMA-VENETOCLAX AND INTENSIVE CHEMOTHERAPY IN ELDERLY AML: SURVIVAL AND SAFETY INSIGHTS FROM GLOBAL MATCHED COHORT

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Introduction

- Acute myeloid leukemia (AML) in older adults is difficult to treat due to frailty and comorbidities that limit tolerance to intensive chemotherapy.
- The standard "7+3" regimen has high toxicity and limited applicability in this group. Venetoclax combined with hypomethylating agents (HMAs) has shown efficacy with improved tolerability in trials, but real-world comparisons with intensive chemotherapy remain limited.

Aim

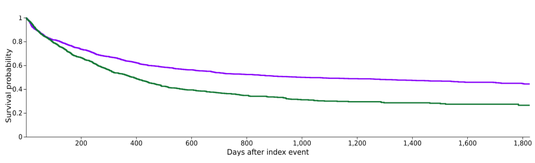
- The aim of this study was to evaluate the real-world outcomes of elderly AML patients treated with HMA-Venetoclax compared to those treated with intensive chemotherapy.

Objectives

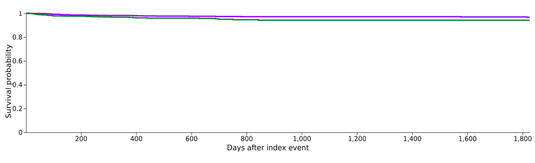
- The primary objective was to compare all-cause mortality between patients receiving HMA-Venetoclax and those receiving intensive chemotherapy.
- Secondary objectives included evaluating hematologic toxicities, infectious complications, cardiac events, ICU-level interventions, organ dysfunction, and transfusion requirements across the two treatment groups.

Methods

- We used the TriNetX global research network to identify AML patients aged 65–75 years treated with either HMA-Venetoclax (azacitidine or decitabine plus Venetoclax) or intensive chemotherapy (cytarabine plus daunorubicin or idarubicin).
- Propensity score matching (1:1) was applied for demographics, comorbidities, and baseline organ function, yielding 1,426 patients per group.
- Outcomes included mortality (primary) and complications (secondary).
- Survival was analyzed with Kaplan–Meier methods, and hazard ratios with 95% confidence intervals were calculated using Cox regression.



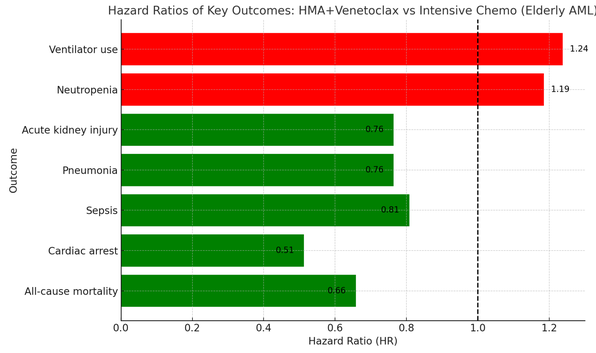
MORTALITY



CARDIAC ARREST

Results

- After matching, 1,426 patients were included in each group.
- Overall survival was significantly better with HMA-venetoclax (HR 0.658; 95% CI 0.591–0.731; p<0.001), reflecting a 34% relative risk reduction.
- Rates of cardiac arrest (HR 0.513; p=0.005), sepsis (HR 0.808; p=0.007), pneumonia (HR 0.764; p=0.001), and acute kidney injury (HR 0.764; p=0.001) were lower with HMA-venetoclax.
- Neutropenia (HR 1.185; p=0.036) and ventilator use (HR 1.238; p=0.023) were more common, though without increased mortality.
- No significant differences were seen for anemia, thrombocytopenia, myocardial infarction, heart failure, fungal/viral infections, thromboembolic events, gastrointestinal complications, or transfusion requirements.



Summary

- In this large real-world matched cohort of elderly AML patients, treatment with HMA-Venetoclax was associated with improved overall survival compared to intensive chemotherapy.
- The regimen was also linked to fewer serious complications, including sepsis, pneumonia, cardiac arrest, and acute kidney injury.
- Although neutropenia and ventilator use were more frequent, these did not translate into higher mortality or greater transfusion requirements.

Discussion

- These findings highlight the clinical value of HMA-Venetoclax as a frontline option for older AML patients, particularly those at higher risk for treatment-related morbidity.
- The improved survival and reduced infectious and cardiac complications observed reinforce results from clinical trials and extend their relevance to routine practice.
- While the increased risk of neutropenia underscores the need for vigilant supportive care, the overall safety and efficacy profile favors the use of HMA-Venetoclax over intensive chemotherapy in this population.

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