

(PS1628) FRONTLINE LOW-INTENSITY VAH ACHIEVES HIGH MRD-NEGATIVE REMISSION RATES IN YOUNGER PATIENTS WITH NEWLY DIAGNOSED AML

Topic: 04. Acute myeloid leukemia - Clinical

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Background

Venetoclax-based combinations have transformed AML treatment, primarily for unfit patients. However, effective frontline options for younger, fit patients remain an unmet need. Homoharringtonine (HHT) shows synergistic activity with both venetoclax and azacitidine. The triplet regimen VAH has demonstrated promise in relapsed/refractory AML, but its efficacy and safety as frontline induction in younger patients are unknown.

Aims

To evaluate the real-world effectiveness and safety of VAH as frontline induction therapy in fit patients aged <65 years with newly diagnosed (ND) AML.

Methods

This single-center retrospective study included 110 consecutive ND AML patients treated with VAH between August 2022 and November 2025 (Table). Eligible patients were 14–65 years with ECOG ≤2. The regimen consisted of venetoclax (100mg d1, 200mg d2, 400mg d3-28), azacitidine (75mg/m² d1-7), and HHT (1mg/m² d1-7) in 28-day cycles. Primary endpoint: composite complete remission (CRc) after cycle 1 (C1). Secondary endpoints: measurable residual disease (MRD) negativity (by MFC, 0.01% threshold), overall survival (OS), event-free survival (EFS), and safety.

Results

The median age was 47 years (range, 14–65); 40% were ELN favorable, 20% intermediate, and 40% adverse risk, reflecting a high-risk real-world population.

After one cycle, CRc rate was 86.4% (95/110), with 69.5% of responders achieving MRD-negativity. Responses deepened after cycle 2 (C2), with CRc increasing to 97.5% (79/81) and MRD-negativity to 83.5% (**Figure**). ELN risk significantly impacted C1 CRc (95.5% favorable, 90.9% intermediate, 75.0% adverse; $P=0.02$) and C2 MRD-negativity (93.9%, 76.5%, 75.9%; $P<0.001$). Multivariable analysis identified ELN non-favorable risk as the sole independent predictor of C1 MRD-positivity (OR 3.21, $P=0.021$). High activity was noted in FLT3-ITD-mutated patients (94.4% C1 CRc). C2 MRD-negativity was strongly associated with superior outcomes.

With a median follow-up of 314 days, estimated 1-year OS and EFS were 86.9% and 73.4%, respectively. EFS was significantly stratified by ELN risk (1-year: 86.5% favorable, 86.4% intermediate, 53.6% adverse; $P<0.01$). Achieving C2 MRD-negativity was associated with significantly superior EFS ($P<0.001$) and OS ($P=0.031$). In multivariable analysis, C1 MRD-positivity (HR 3.90, $P=0.001$) and ELN risk (HR 2.12, $P=0.003$) were independent predictors of inferior EFS.

Grade ≥3 hematologic toxicities were frequent but manageable: neutropenia (91.8%), febrile neutropenia (36.4%), with two infection-related deaths (1.8%).

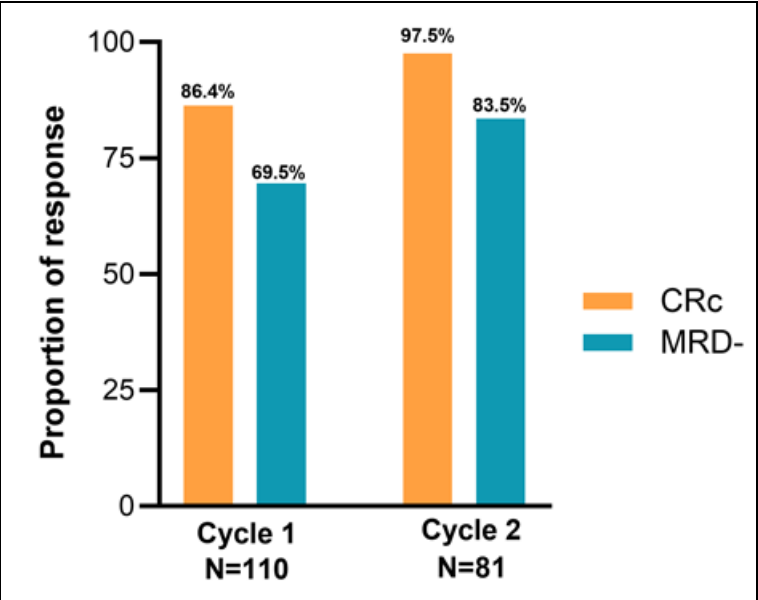
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Summary/Conclusion

Frontline VAH is a highly effective and tolerable induction regimen for fit patients with ND AML, achieving rapid and deep MRD-negative remissions across ELN risk groups, including adverse-risk and FLT3-ITD-mutated disease. Early molecular response translated into favorable 1-year survival. These real-world data support further prospective evaluation of VAH as a frontline induction strategy.



Rapid and Deep Responses Achieved with Frontline VAH in Newly Diagnosed AML

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