Venetoclax in Combination with a Hypomethylating Agent (Ven+HMA) for Patients with Newly-Diagnosed (ND) Acute Myeloid Leukemia (AML) Who are Medically Unfit for Intensive Induction Therapy: A Real-World, Community Experience

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Background

- Venetoclax in combination with a hypomethylating agent (Ven+HMA) is the current standard of care (SOC) for patients with newly-diagnosed (ND) acute myeloid leukemia (AML) unfit for intensive chemotherapy
- The pivotal VIALE-A trial[1] demonstrated an improved overall survival (OS) with Ven+HMA versus HMA alone, but some patients may not have truly been unfit, as eligibility criteria included ECOG performance status (PS) 0-2 and good organ function
- Over half of patients on the VIALE-A trial had ECOG of 0-1
- At our institution, we use the "treatment-related mortality" (TRM) model as an objective and reproducible measure of unfitness, which combines PS with clinical and disease-related varia les to predict 28-day mortality following intensive chemotherapy[2]
- As a second criticism, most trial patients received treatment at tertiary care centers, limiting the generalizability of the findings to the regimen's current widespread use in community settings for patients who likely do not otherwise meet the rigorous clinical trial eligibility criteria

Objectives

To evaluate the efficacy, toxicity, healthcare resource utilization, and qualify of life outcomes (QOL) in objectively unfit patients with ND AML treated with Ven+HMA in community oncology settings

Methods

- Patients with ND AML with high TRM scores (≥ 13.1, corresponding to an ≥ 13.1 risk of mortality following intensive induction chemotherapy[2]) planning to receive Ven+HMA in the community setting were identified and followed prospectively
- Ven+HMA was administered as per SOC
- Physicians were given a questionnaire inquiring about the treatment decision process
- Patients received the EORTC QLQ-C30 to assess QOL
- Other patient outcomes were tracked via the electronic medical record

Outcome Measures

Primary: Complete remission rate (CR)
Secondary: OS, QOL, rate of febrile neutropenia, healthcare resource utilization, ICU utilization, blood product utilization, and physician decisions regarding treating unfit AML patients

Results

- 30 patients enrolled from 2/2020-2/2026 receiving a median (range) of 3 (1-14) cycles of Ven+HMA

Table 1 describes baseline patient characteristics

- The median age was 76 (30-88) years, and median baseline TRM scores were high at 20.5 (14.8-53.9)

Outcomes are described in Table 2

- 12 patients (40%, 95% CI: 10-42%) achieved CR as best response and 7 (23%) achieved CRi for ORR of 63%
- Physicians independently made the final decision regarding the treatment regime for 5 patients (17%), 7 patients determined their own treatment course (23%), and in the majority (47%) it was a joint decision
- In surveys, physicians expected CR as the outcome for 50% of patients and chose Ven+HMA because patients were too old (30%) or too frail (67%) for intensive therapy, patients worried about toxicity (53%), and/or patients wanted to be treated in an outpatient setting (47%)
- 2/3 patients discontinued therapy due to toxicity or frailty-related factors
- The median OS was 9.96 months (95% CI 5.8-33.8; **Figure 1**) and 12-month OS 45% (25-62%)
- Quality of life and resource utilization data are still undergoing analysis

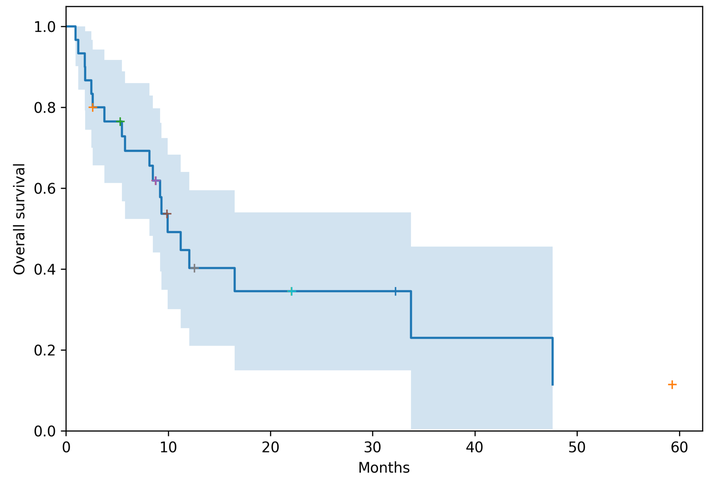
Table 1: Baseline Patient Characteristics

Characteristics, median (range)	Cohort (N = 30)
Age (years)	76 (30-88)
Baseline TRM score	20.5 (14.8-53.9)
Baseline WBC (10^3/μL)	5.3 (0.4-64)
ECOG Performance Status	2 (1-3)
Secondary Disease	12 (40%)

Table 2: Patient Outcomes

Clinical Outcomes, n (%)	Cohort (N = 30)
Number of Ven+HMA cycles, median (range)	3 (1-14)
Complete Remission (CR)	12 (40%)
CR with Incomplete Hematologic Recovery (CRi)	7 (23%)
Resistant Disease	6 (20%)
30-Day Mortality	1 (3.3%)
60-Day Mortality	4 (13.3%)

Figure 1: Patient Survival on Ven+HMA



Conclusions

- While CR rates were similar to those reported in VIALE-A (40% vs. 37%), this was not reflected in survival, with OS being substantially shorter in our unfit cohort (10 vs. 14.7 months),
- These data suggest that clinical trial definitions of "unfit" underestimate frailty of patients treated in community settings
- This data should be considered when counseling patients on expected outcomes following Ven+HMA
- **Further trials are needed to optimize patient selection, dosing and supportive care approaches to reduce toxicity of Ven+HMA in frail, real-world patients**

References

1. DiNardo CD et al. N Engl J Med 2020;383:617-629
2. Walter RB et al. J Clin Oncol. 2011 Nov 20;29(33):4417-23

Acknowledgement

This trial was conceived and designed in part by Elihu Estey, who died in 2021. It was funded by generous contributions from the South Sound CARE Foundation, dedicated to providing clinical trials to oncology patients in their own community.