Weekly Metronomic HMA + Venetoclax in Older Adults with Myeloid Neoplasms: A Real-World Experience

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INTRODUCTION

- HMA + venetoclax (VEN) is standard of care for older or unfit AML: **VIALE-A** reported cCR ~66% and median OS 14.7 months.[1]
- Standard 28-day VEN causes prolonged myelosuppression and heavy transfusion needs — limiting use in frail, comorbid, or transfusion-restricted patients.[1]
- Metronomic weekly dosing + all-oral decitabine-cedazuridine (DEC-C) enables flexible, outpatient, low-intensity delivery.[2], [3]

AIM

- To describe real-world clinical outcomes with weekly metronomic HMA + VEN in an older, heavily comorbid myeloid-neoplasm cohort at a single center.
- Outcomes assessed included response rate, overall survival, event-free survival, treatment duration, transfusion independence, and grade 3–4 therapy-related cytopenias.

METHOD

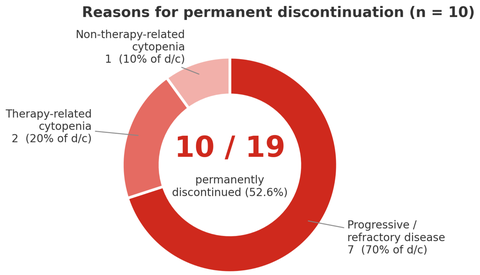
- **Design:** Retrospective single-center review (Mayo Clinic, Jacksonville, FL)
- **Cohort:** 19 patients, 16 AML, 2 MDS-IB, 1 CMML, treated July 2024 to October 2025
- **Regimen:** Weekly HMA + VEN; VEN dose adjusted for CYP3A4 inhibitors
- **Response:** ELN 2022 AML criteria[4]
- **Risk:** ELN 2024 for less-intensive therapies[5]

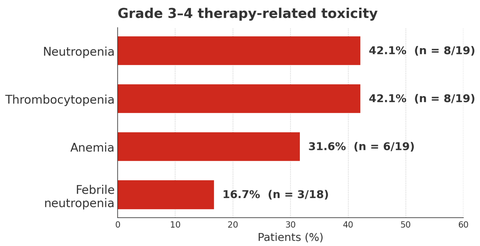
CONCLUSIONS

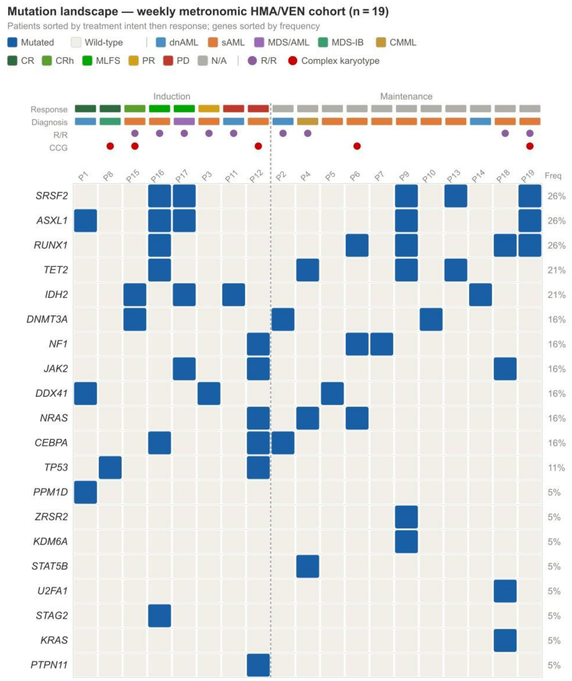
- Weekly metronomic HMA + VEN, delivered predominantly as an all-oral regimen — was clinically active in an older, heavily pretreated, high-comorbidity population.
- Attenuated myelosuppression and outpatient convenience make this approach applicable in frail patients and transfusion-restricted populations.

RESULTS

- **Cohort.** Nineteen patients (16 AML, 4 de novo, 12 sAML/MRC/tAML; 2 MDS-IB1/2; 1 CMML) were treated between July 2024 and October 2025. Median age was **79 years (range 68–90)**, with a median of 2 comorbidities (range 0–7). ECOG PS was 0–1 in 66.7% and 2–3 in 33.3%.
- **Regimen.** Weekly HMA + VEN was delivered as induction in 8 patients (42.1%) and as maintenance after standard-dose HMA/VEN in 11 (57.9%). Seventeen patients (89.5%) received **all-oral decitabine/cedazuridine 35/100 mg + VEN weekly**; 1 received subcutaneous decitabine 0.2 mg/kg + VEN; 1 received IV decitabine 20 mg/m² + VEN.
- **Response and survival.** Median treatment duration was 21.6 weeks (range 1–64). Median time to response was 2.9 months. Median overall survival was 11.7 months (median follow-up 9.3 months); median event-free survival was 10.4 months. Seven deaths occurred, all disease-related.







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REFERENCES

1. **DiNardo CD, et al.** Azacitidine and venetoclax in previously untreated AML. *N Engl J Med*. 2020;383(7):617–629.
2. **Levitz D, et al.** A metabolically optimized, noncytotoxic low-dose weekly decitabine/venetoclax in MDS and AML. *Clin Cancer Res*. 2023;29(15):2774–2780.
3. **Zeidan AM, et al.** All-oral DEC-C + venetoclax in newly diagnosed AML: phase 2 (ASCERTAIN-V). *J Clin Oncol*. 2025;43(16_suppl):6504.
4. **Döhner H, et al.** Diagnosis and management of AML in adults: 2022 ELN recommendations. *Blood*. 2022;140(12):1345–1377.
5. **Döhner H, et al.** Genetic risk classification for adults with AML receiving less-intensive therapies: 2024 ELN. *Blood*. 2024;144(21):2169–2173.
6. **Gangat N**, Tefferi A. Venetoclax schedule in AML: 7 vs 14 vs 21 vs 28 days. *Blood Cancer J*. 2025;15(1):56.
7. **Bock AM**, Pollyea DA. Venetoclax with azacitidine in Jehovah's Witness patients with high-risk AML. *Am J Hematol*. 2020;95(10):E269–E272.