VENETOCLAX AND AZACITIDINE THERAPY IN ACUTE MYELOID LEUKEMIA PATIENTS WITH SEVERE RENAL IMPAIRMENT: A RETROSPECTIVE COHORT PROPENSITY SCORE-MATCHED ANALYSIS

ADITI CHITTETI MD[1], ANSY PATEL MD[1], VEDANT SHAH MD[2] AND JOEL ALCID MD[2]
1. SUNY UPSTATE MEDICAL UNIVERSITY, SYRACUSE, NY, USA
2. THE NEW YORK MEDICAL COLLEGE, DENVILLE, NJ, USA

INTRODUCTION

Venetoclax combined with hypomethylating agents (VEN/HMA) is the standard of care for older/unfit patients with AML, yet patients with severe renal impairment were excluded from the pivotal VIALE-A trial.

AIMS

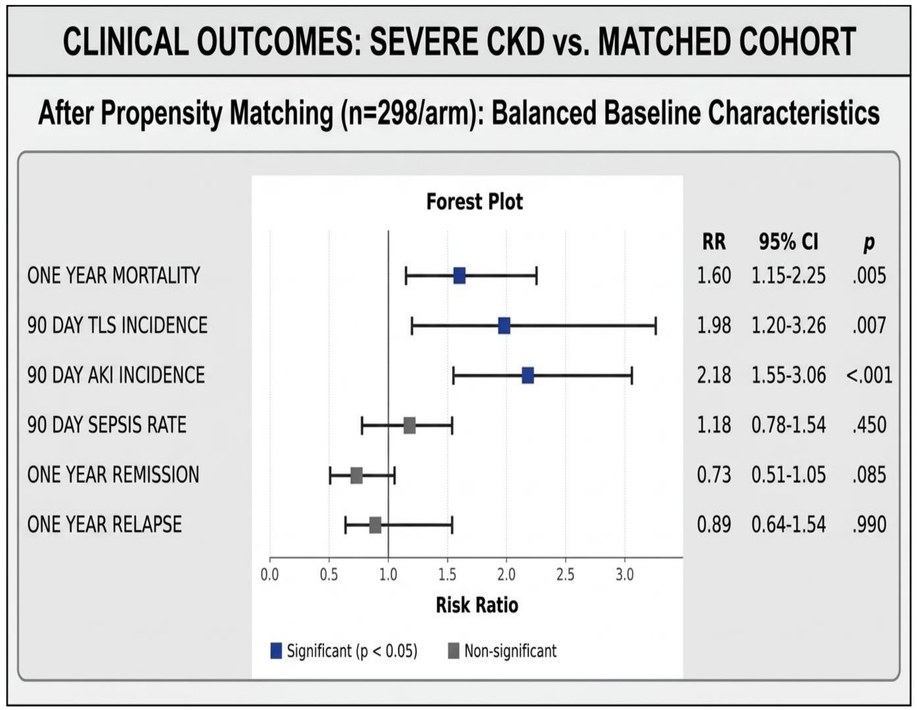
Pharmacokinetic data suggest no dose adjustment is required for CrCl ≥15 mL/min, but clinical outcomes data in this population remain limited to small retrospective series. We aimed to evaluate the safety and efficacy of VEN/HMA in AML patients with pre-existing severe CKD.

METHODS

- Using the TriNetX Global Network, we identified adults with newly diagnosed AML who received venetoclax with azacitidine or decitabine (initiated within 14 days).
- Two cohorts were defined: Severe CKD (CKD stage 3b, 4, 5, ESRD diagnosed on or before AML diagnosis; n=302) and No Severe CKD (absence of these diagnoses; n=6,291).
- 1:1 propensity score matching (PSM) was performed for demographics (age, sex, race, ethnicity), comorbidities (HTN, IHD, CVA, HF, COPD, DM), baseline laboratory values (leukocytes, platelets, erythrocytes, LDH), and prior HMA exposure.
- Outcomes included 1-year overall survival (OS); 90-day tumor lysis syndrome (TLS), acute kidney injury (AKI), and sepsis; and 1-year remission and relapse rates; calculated from first VEN/HMA administration.

RESULTS

- One year mortality was significantly higher in the severe CKD cohort (57.9% vs. 46.3%; RR 1.25, 95% CI 1.07–1.46; OR 1.60, 95% CI 1.15–2.21; p=0.005).
- Ninety-day TLS incidence was significantly elevated (16.4% vs. 9.1%; RR 1.82, 95% CI 1.17–2.82; OR 1.98, 95% CI 1.20–3.26; p=0.007).
- Ninety-day AKI was markedly more frequent (45.6% vs. 27.9%; RR 1.64, 95% CI 1.31–2.04; OR 2.18, 95% CI 1.55–3.06; p0.001).
- Ninety-day sepsis rates were comparable (25.8% vs. 24.2%; p=0.45).
- One-year remission trended lower insignificantly in the CKD cohort (31.4% vs. 38.6%; OR 0.73, 95% CI 0.51–1.05; p=0.085)
- 1-year relapse wasn't significantly different (22.8% vs. 22.9%; p=0.99).



CONCLUSION

In this propensity score-matched real-world analysis, AML patients with severe CKD treated with VEN/HMA demonstrated significantly higher one-year mortality, 90-day TLS, and 90-day AKI compared to those without severe CKD, despite pharmacokinetic data indicating no dose adjustment is required. These findings underscore need for intensified TLS prophylaxis, renal monitoring, and consideration of dose modifications in this vulnerable population.

CONTACT INFORMATION

ADITI.CHITTETI@GMAIL.COM

REFERENCES

• DiNardo CD, Jonas BA, Pullarkat V, Thirman MJ, Garcia JS, Wei AH, et al. Azacitidine and venetoclax in previously untreated acute myeloid leukemia. N Engl J Med. 2020;383(7):617-29.
• Agarwal SK, Salem AH, Danilov AV, Hu B, Puvvada S, Gutierrez M, et al. Effect of renal impairment on the pharmacokinetics of venetoclax in patients with chronic lymphocytic leukemia. Cancer Chemother Pharmacol. 2017;80(1):163-9.