MRD-Guided Risk Stratification in Venetoclax-Treated Newly Diagnosed AML: A Pooled Survival Analysis

T. Nihal[1], A. Nawal[2], A. Azhar[3], J. Ahmed[4], A. Farooq[8], M. Sherwani[6], N. Tamanna[7], A. Hassan[8], F. Ansari[9], S. Qasim[10] and H. Bin Khalid[11]

1. Allama Iqbal Medical College, Lahore, Pakistan
2. Khawaja Muhammad Safdar Medical College, Sialkot, Pakistan
3. Detroit Medical Center/Wayne State University, USA
4. Northwest Health Porter, Valparaiso, Indiana, USA
5. King Edward Medical University, Lahore, Pakistan
6. Duke University Hospital, Durham, NC, USA
7. Department of Internal Medicine, Suny Upstate Medical University, Syracuse, NY, USA
8. Hackensack Meridian Jersey Shore University Medical Center, Neptune, NJ, USA
9. Loma Linda University Faculty Medical Group - Department of Internal Medicine, Loma Linda, USA
10. Ameer-ud-Din Medical College, Post Graduate Medical Institute, Lahore, Pakistan
11. Geisinger Health System, PA, Wilkes-Barre, USA

Hackensack Meridian *Health*
Jersey Shore University Medical Center

BACKGROUND

Venetoclax combined with hypomethylating agents has emerged as frontline therapy for older or unfit patients with newly diagnosed acute myeloid leukemia (AML). Although measurable residual disease (MRD) is a validated prognostic marker in intensively treated AML, its prognostic impact in venetoclax-based regimens has not been comprehensively quantified. We performed a pooled survival analysis to evaluate the association between MRD negativity and clinical outcomes in this setting.

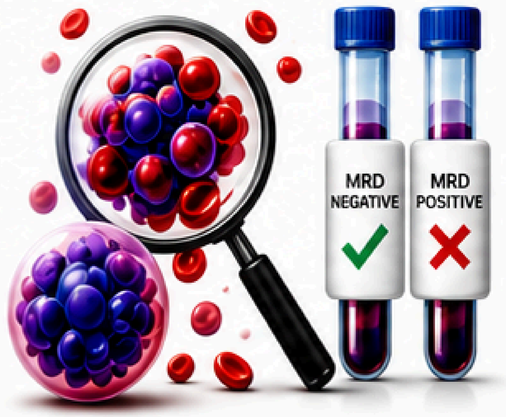
AIM

To evaluate the association between MRD negativity and survival outcomes in newly diagnosed AML patients treated with venetoclax-based therapy.

METHODS

- A systematic search identified prospective trials and real-world cohorts reporting survival outcomes stratified by MRD status in newly diagnosed AML treated with venetoclax-based therapy.
- Studies providing hazard ratios (HRs) or extractable Kaplan–Meier curves were included.
- When HRs were not directly reported, they were reconstructed using established time-to-event estimation methods.
- Random-effects modeling was applied.
- Heterogeneity was assessed using the I^2 statistic.

CONCLUSIONS



MRD negativity following venetoclax-based frontline therapy is strongly associated with superior survival and reduced relapse risk in newly diagnosed AML. Despite moderate methodological heterogeneity and varying MRD platforms, the prognostic signal was consistent across studies. These findings support incorporation of MRD assessment into response evaluation and risk-adapted therapeutic strategies in venetoclax-treated AML and highlight the need for prospective MRD-guided clinical trials.

RESULTS

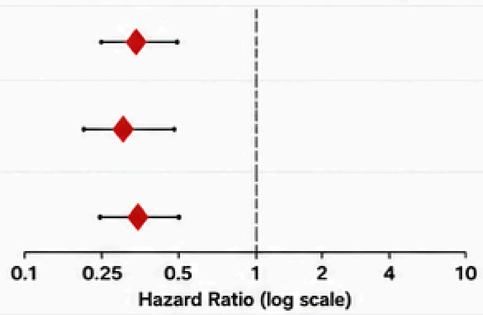
9 STUDIES

742 PATIENTS

MRD assessment was primarily performed using multiparameter flow cytometry with sensitivity thresholds ranging from 10^{-3} to 10^{-4}.

MRD negativity was strongly associated with improved survival outcomes across all endpoints.

Outcome	Pooled HR (95% CI)	Forest Plot (Hazard Ratio)	Favors MRD Negative	Favors MRD Positive
Overall Survival (OS)	0.48 (0.36–0.63)		✓	
Relapse-free / Progression-free Survival (RFS/PFS)	0.44 (0.31–0.61)		✓	
Cumulative Incidence of Relapse (CIR)	0.52 (0.38–0.71)		✓	



All effects were statistically significant ($p<0.001$) with low to moderate heterogeneity across outcomes (OS: I^2=32%; RFS/PFS: I^2=35%; CIR: I^2=28%).

Sensitivity analyses and leave-one-out analyses confirmed robustness of results.

ACKNOWLEDGEMENTS

None.

CONTACT INFORMATION

Phone No: +1(203) 571-9463.

REFERENCES

1. Nachmias B, Haran A, Yisraeli Salman M, Stein EM. Measurable residual disease–guided therapy in acute myeloid leukaemia: Practical insights. British Journal of Haematology. 2025 Oct;207(4):1192-212.
2. Bernardi M, Ferrara F, Carrabba MG, Mastaglio S, Lorentino F, Vago L, Ciceri F. MRD in Venetoclax–based treatment for AML: Does it really matter?. Frontiers in oncology. 2022 Jul 18;12:890871.