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SAFETY, EFFICACY, AND PREDICTIVE FACTORS OF VENETOCLAX-BASED REGIMENS IN ELDERLY ACUTE MYELOID LEUKEMIA PATIENTS: A META-ANALYSIS

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INTRODUCTION

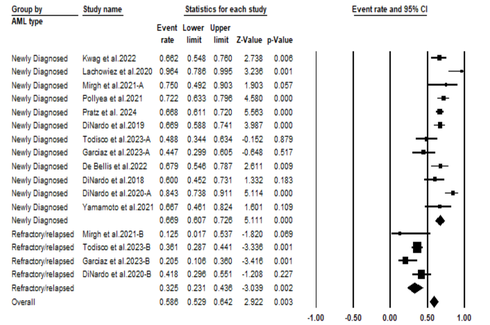
The prognosis for elderly patients with acute myeloid leukemia (AML) remains poor due to the aggressive nature of the disease and the limitations of conventional chemotherapy, which is often not well tolerated in this population. Venetoclax, a BCL-2 inhibitor, has emerged as a promising treatment option when combined with low-intensity therapies such as hypomethylating agents (HMAs) or low-dose cytarabine (LDAC). This meta-analysis aims to synthesize current evidence on the safety, efficacy, and predictive factors for response to Venetoclax-based regimens in elderly AML patients.

METHOD

- A comprehensive search for literature related to our study objective was performed on PubMed, Embase, Web of Science, and Google Scholar databases. The statistical analyses were performed using Review Manager or the Comprehensive Meta-Analysis software. In addition, methodological quality evaluation of non-randomized studies was conducted using the Newcastle Ottawa Scale, while bias assessment of randomized studies was performed with Cochrane's risk of bias tool.

RESULTS

12 studies, including 1432 elderly AML patients treated with venetoclax-based regimens, were identified for review and analysis. The pooled analysis showed that the rate of complete response with or without incomplete blood count recovery (CR/CRi) and overall response rate (ORR) among patients treated with venetoclax and HMAs was 59% and 64%, respectively. On the other hand, an ORR of 50% was observed in patients treated with venetoclax and LDAC. Furthermore, venetoclax and HMAs demonstrated a significant survival benefit (HR: 0.57; 95% CI: 0.47 – 0.68; p<0.00001). The most common grade 3 or greater hematologic disorder in AML patients treated with Venetoclax and HMAs was febrile neutropenia (39%). In comparison, thrombocytopenia was more common in patients treated with venetoclax and LDAC (41%).

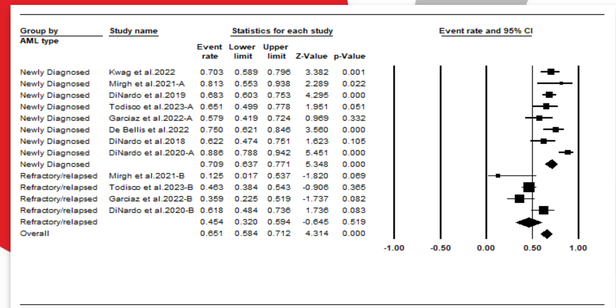


Forest plot showing the rate of CR/CRi in patients treated with venetoclax plus HMAs stratified according to disease status

Outcome	Subgroup	No. of studies	Effect size (95% CI)	p-value	I^2(%)
OS	VEN plus HMAs vs. HMAs plus placebo	3	0.58 (0.48 – 0.70)	<0.00001	0
	VEN plus HMAs vs. Intensive chemotherapy	1	0.32 (0.12 – 0.83)	0.02	N/A
ORR	ND AML	8	0.71 (0.64 – 0.77)	0.001	57.24
	R/R AML	4	0.45 (0.32 – 0.59)		68.53
CR/CRi	ND AML	12	0.70 (0.61 – 0.73)	<0.0001	65.75
	R/R AML	4	0.33 (0.23 – 0.44)		51.34
	TP53	3	0.56 (0.42 – 0.69)	0.003	32.47
	FLT3	3	0.57 (0.40 – 0.72)		45
	IDH1/2	3	0.74 (0.62 – 0.82)		9.51
	NPM1	3	0.85 (0.74 – 0.91)		0

CONCLUSIONS

In summary, venetoclax combined with HMAs or LDAC demonstrated promising efficacy and a tolerable safety profile in elderly patients with AML. Moreover, venetoclax and HMAs showed significant survival benefits among elderly AML patients. However, this finding was based on retrospective data. Therefore, large-sample prospective trials are required to support this finding. Furthermore, TP53 and FLT3 mutations, R/R AML, and adverse cytogenetics predicted poor response rates in patients treated with venetoclax combined with HMAs. Conversely, TP53 and FLT3 mutations, adverse cytogenetics, and secondary AML predicted poor response rates in patients treated with venetoclax combined with LDAC.



Forest plot showing the rate of CR/CRi in patient treated with venetoclax plus HMAs stratified according to somatic mutations

REFERENCES

1. Chaurasiya PS, Lamsal DK, Khatri A, et al. Prevalence of acute myeloid leukemia and its associated risk factors at a tertiary care center: a retrospective cross-sectional study. Ann Med Surg (Lond). 2023;85(10):4794-4798. doi:10.1097/MS9.0000000000001189

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