Prognostic performance of ELN 2024 and Mayo Clinic 2025 risk classifications in older patients with acute myeloid leukemia treated with first-line azacitidine and venetoclax at a secondary care hospital.

Ane Brieva López[1], María Ordóñez García[1], Mariana Cerrato Salas[1], Pavel Manuel Acevedo Pérez[1], Juan Sastre Ortega[1] , Juan Carlos Tenécora Quito[1], Esther Jaro Arias[1], Alicia Lorenzo Jambrina[1], Jorge Sánchez- Calero Guillarte[1], M Ángeles Andreu Costa[1].

1. Hospital Universitario de Móstoles. Madrid. España.

INTRODUCTION

The European Leukemia Net (ELN) 2017 and 2022 risk classifications for acute myeloid leukemia (AML) were developed in patients receiving intensive chemotherapy and have limited prognostic value in older patients treated with lower-intensity regimens. Following the VIALE-A trial, azacitidine plus venetoclax (AZA/VEN) became standard therapy, prompting development of ELN 2024 and Mayo Clinic 2025 classifications for AZA/VEN-treated patients.

Aim: To assess outcomes and compare prognostic performance of ELN 2024 versus ELN 2017, ELN 2022, and Mayo Clinic 2025 in older AML patients receiving first-line AZA/VEN.

RESULTS

Median age was 74 years, and 33% had secondary AML. RUNX1 and IDH2 mutations were most frequent (33% each), followed by DNMT3A (26%) and NPM1 (20%) (Table 1). ELN 2024 classified 11 patients as favorable risk, whereas Mayo Clinic 2025 assigned nine patients to intermediate risk, reclassifying eight ELN 2024 favorable-risk cases (Figure 1). After median follow-up of 62 months, median OS and PFS were 40 and 27 months. Median OS with ELN 2024 was 57, 18, and 24 months for favorable, intermediate, and adverse groups, while Mayo Clinic 2025 provided better survival discrimination, with median OS not reached in the favorable group (Figure 2). Overall, 66% achieved measurable residual disease-negative complete remission after median four treatment cycles and became transfusion independent.

Age at diagnosis (median)		74
Sex (%)		80% M / 20% F
Secondary AML (%)		33.30%
Hb at diagnosis, g/L (median)		95 IQR 81–126
N at diagnosis, ×10^9/L (median)		0.5 IQR 0.3–1.3
Plt at diagnosis, ×10^9/L (median)		108 IQR 28–151
Karyotype (%)	Normal	53.3% (n=8)
	Complex	20% (n=3)
	Tri18, del17p	6.6% (n=1)
	t(8;21)	6.6% (n=1)
NGS	NPM1	20% (n=3)
	TET2	13% (n=2)
	IDH2	33% (n=5)
	DNMT3A	26% (n=4)
	CBF::MYH11	6.6% (n=1)
	FLT3	0%
	RUNX1	33% (n=5)
	EZH2	6.6% (n=1)
	ASXL1	6.6% (n=1)
	SRSF2	20% (n=3)
	P53	13.3% (n=2)
ELN 2017 risk (F/I/A)		F 4 / I 2 / A 9
ELN 2022 risk (F/I/A)		F 4 / I 1 / A 10
ELN 2024 risk (F/I/A)		F 11 / I 2 / A 2
Mayo Clinic 2025 risk (F/I/A)		F 4 / I 9 / A 2
WHO 2022	AML with CBF::MYH11 fusion	6.60% (n=1)
	AML with RUNX1::RUNX1T1 fusion	6.60% (n=1)
	AML with NPM1 mutation	13.3% (n=2)
	AML with other genetic alterations	6.60% (n=1)
	Myelodysplasia-related AML	53.3% (n=8)
	MDS-IB2	13.3% (n=2)
ICC 2022	AML with recurrent genetic abnormalities	26.6% (n=4)
	AML with myelodysplasia-related gene mutations	46.6% (n=7)
	MDS/AML with cytogenetic abnormalities	6.60% (n=1)
	AML with TP53 mutation	6.60% (n=1)
	MDS/AML with TP53 mutation	6.60% (n=1)
	MDS/AML, NOS	6.60% (n=1)
CR		66.6% (n=10)
Median cycles to CR		4 IQR 3–6
MRD negative		66.6% (n=10)
Median cycles to MRD negativity		4 IQR 3–6

Table 1. Clinical, biological, and treatment-response characteristics of the study cohort

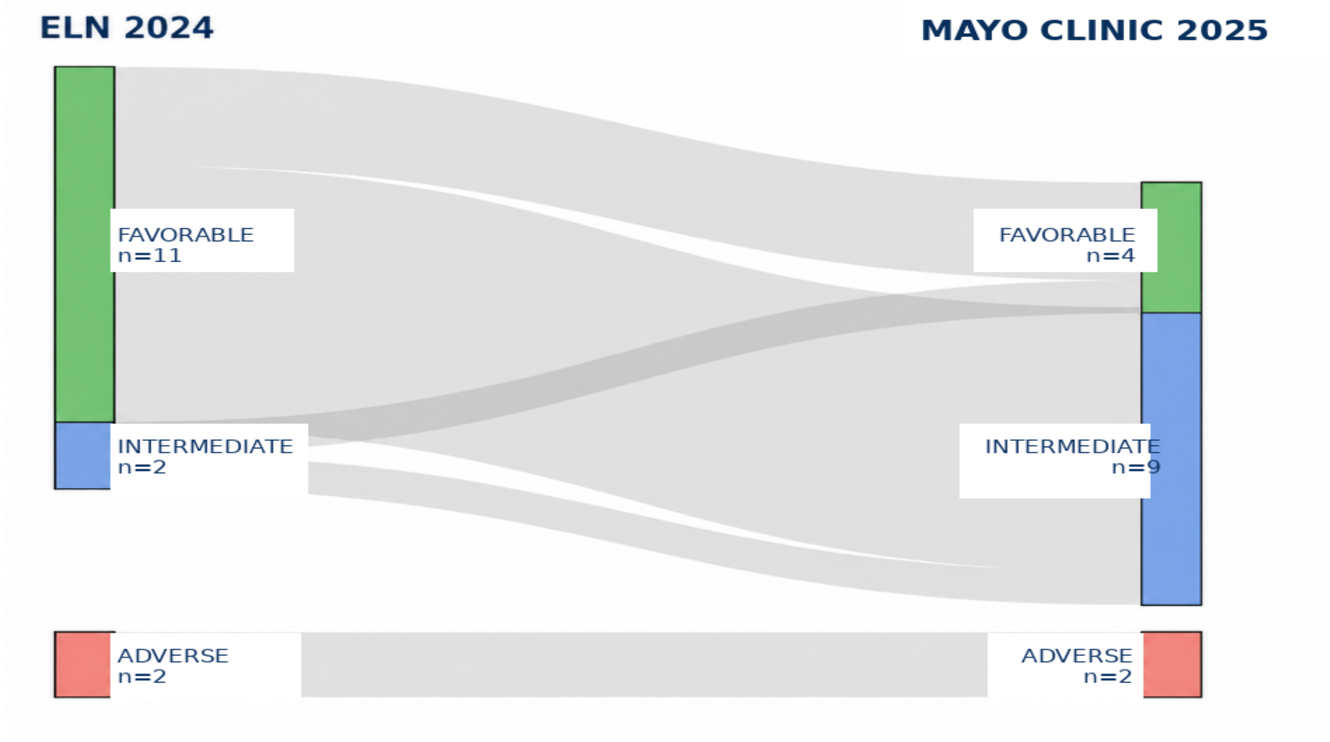

Figure 1. Prognostic reclassification according to ELN 2024 and Mayo Clinic 2025 in the study cohort.

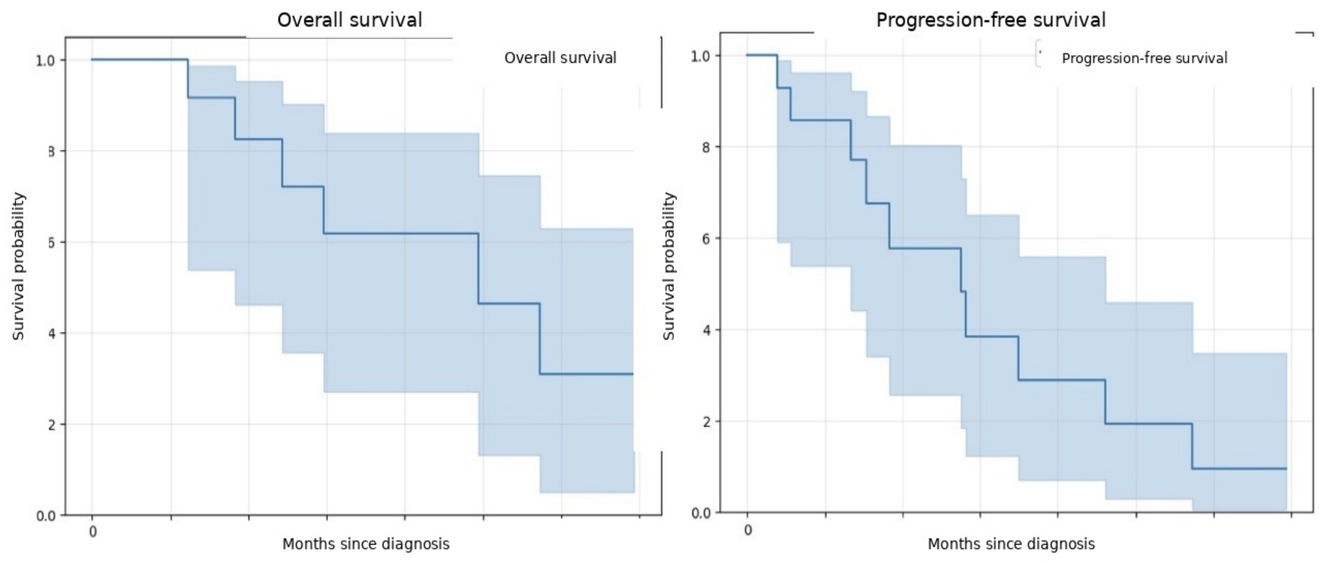

Figure 2. Kaplan–Meier survival analysis of the study cohort.

CONCLUSION

ELN 2024 recognizes favorable prognostic effects of NPM1, IDH1/2, and DDX41 mutations without signaling pathway alterations, classifying many AZA/VEN-treated patients as favorable risk. Mayo Clinic 2025 additionally incorporates adverse cytogenetics and KMT2A, TP53, and KRAS mutations in IDH2 wild-type disease, reclassifying many patients as intermediate risk. Despite the small cohort, these findings support AZA/VEN-specific prognostic models over classifications developed for intensive chemotherapy.

REFERENCES

1. Döhner H et al. Genetic risk classification for adults with AML receiving less-intensive therapies: the 2024 ELN recommendations. Blood. 2024;144 (2):2169-2173

2. DiNardo CD et al. Azacitidine and Venetoclax in previously untreated acute myeloid Leukemia. N Engl J Med. 2020; 383(7):617-629.

3. Gangat N et al. Mayo Genetic Risk Models for Newly Diagnosed Acute Myeloid Leukemia Treated With Venetoclax + Hypomethylating Agent**.** American Journal of Hematology. 2025;100:260-271

CONTACT

Ane Brieva López. brievalopezane@gmail.com

www.iachlive.cme-congresses.com

IACH

www.iachlive.cme-congresses.com