MENIN INHIBITORS vs FLT3 INHIBITOR-BASED THERAPY IN NPM1-MUTATED RELAPSED/REFRACTORY AML: COMPARATIVE EFFICACY, MRD DEPTH, AND SAFETY PROFILES

Hashem Haj Ebrahimi[1], Hiam Ghunaim[1], Fakriyeh Abachi Nejad Asl[2]

[1] Hennepin Healthcare, Minneapolis, MN, USA | [2] University of Debrecen, Debrecen, Hungary

BACKGROUND

NPM1-mutated relapsed/refractory AML is driven by HOXA/MEIS transcriptional addiction and frequent FLT3 co-mutation. Two therapeutic paradigms have emerged: FLT3 inhibitor (FLT3i)-based kinase blockade and menin inhibition (MENi) targeting transcriptional dependency.

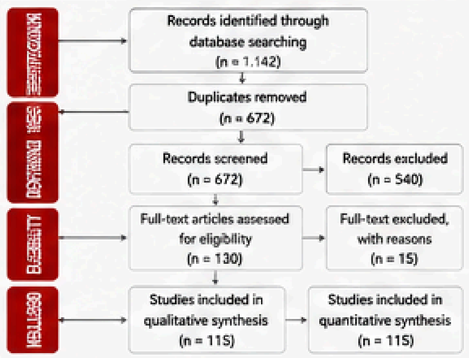
OBJECTIVE

To compare efficacy and safety of MENi vs FLT3i-based regimens in NPM1-mutated relapsed/refractory AML using a systematic review of early clinical data.

METHODS

- Systematic review of PubMed and Embase (2019–2026) following PRISMA guidelines
- Screening performed using Rayyan.ai
- Phase 1/2 trials and retrospective cohorts reporting NPM1-mutated outcomes included
- Median follow-up: 4–18 months
- Data synthesized using descriptive study-level aggregation
- Settings: Multicenter academic and tertiary referral centers across North America, Europe, and Asia

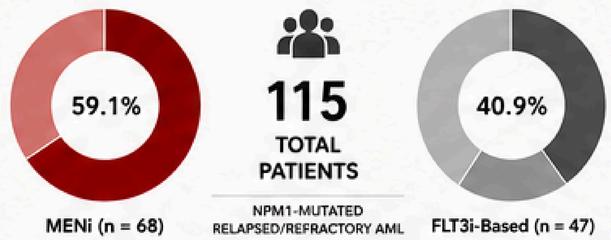
PRISMA FLOW DIAGRAM



STUDY AT A GLANCE

- **115** TOTAL PATIENTS
- **68** MENi (Revumenib, Ziftomenib)
- **47** FLT3i-BASED (Gilteritinib ± combo)

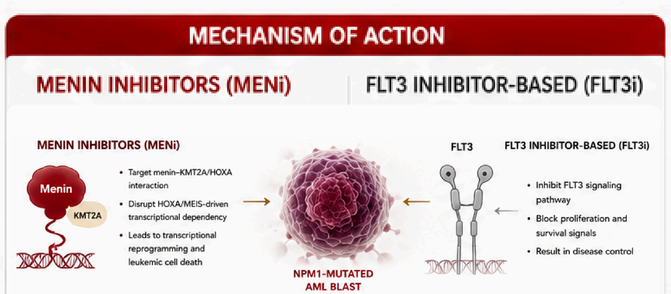
PATIENTS & DISEASE CHARACTERISTICS



PATIENT CHARACTERISTICS (OVERALL)

Median Age		Median Prior Lines of Therapy	Median Follow-up
61 years (range 22–78)	61.2% ♂	2 (range 1–5)	10.2 months (range 4–18)

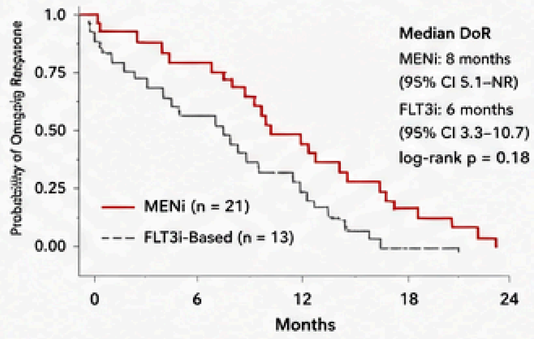
MECHANISM OF ACTION



EFFICACY OUTCOMES

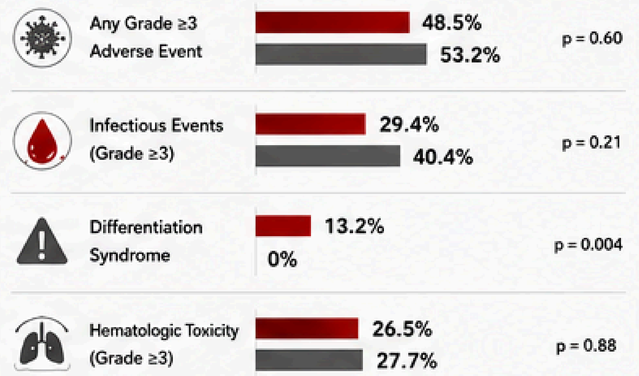
MENi (n = 68)	OUTCOME	FLT3i-BASED (n = 47)
32/68 (47.1%)	Overall Response Rate (ORR)	20/47 (42.6%)
21/68 (30.9%)	Complete Response/ CRi	13/47 (27.7%)
12/21 (57.1%)	MRD Negativity (among evaluable responders)	6/20 (30.0%)
8 months	Duration of Response (DoR, median)	6 months

DURATION OF RESPONSE (DoR)



SAFETY & TOXICITY

INCIDENCE OF GRADE ≥3 ADVERSE EVENTS



OTHER SAFETY OUTCOMES

TREATMENT DISCONTINUATION RATE

STOP

7.4% (5/68)

8.5% (4/47)

p = 0.72

ICU ADMISSIONS (GRADE ≥3 EVENTS)

5.9% (4/68)

8.5% (4/47)

KEY TAKEAWAY

MENi and FLT3i-based regimens show comparable remission rates in NPM1-mutated relapsed/refractory AML but differ in response depth. MENi achieves deeper MRD negativity, while FLT3i is associated with higher infectious burden and broader disease control. MENi is associated with differentiation syndrome. These data define biologically distinct response trajectories and support optimized sequencing strategies in NPM1-mutated AML.

DISCLAIMER: AI was used to assist with the creation of diagrams.

CONCLUSIONS

MENi and FLT3i-based regimens demonstrate comparable remission rates in NPM1-mutated relapsed/refractory AML but differ in response depth. MENi shows higher MRD negativity. FLT3i provides broader disease control with higher infectious burden, while MENi is associated with differentiation syndrome. These data support optimized sequencing strategies in NPM1-mutated AML.

ABBREVIATIONS

AML: acute myeloid leukemia; CR: complete remission; CRi: complete remission incomplete; DoR: duration of response; FLT3: fms-related tyrosine kinase 3; HOXA: homeobox A; MEIS: MEIS homeobox; MRD: measurable residual disease; NPM1: nucleophosmin 1; ORR: overall response rate; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Hennepin Healthcare

UNIVERSITY of DEBRECEN