

Risk of Progression to Acute Myeloid Leukemia Among Patients with Myelodysplastic Syndromes and Type 2 Diabetes Treated With GLP-1 Receptor Agonists

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INTRODUCTION

- Glucagon-like peptide-1 receptor agonists (GLP-1RA) possess anti-inflammatory and immunomodulatory properties that may influence malignant hematopoiesis.¹
- However, whether GLP-1RA exposure is associated with risk of progression from myelodysplastic syndromes (MDS) to acute myeloid leukemia (AML) among patients with T2D remains unknown.

AIM

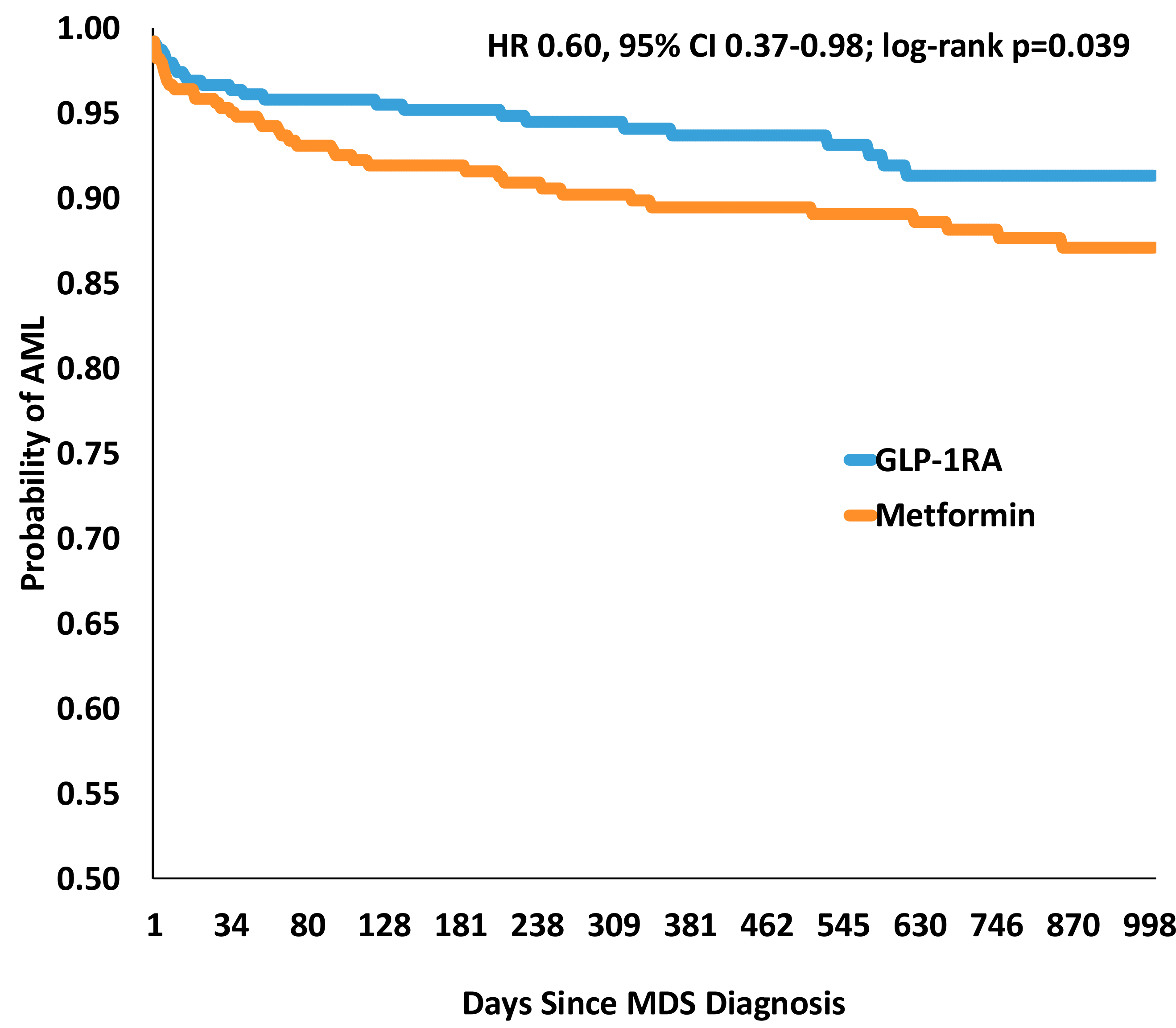
- To evaluate the association between GLP-1RA exposure and risk of progression to AML among patients with MDS and T2D.

METHODS

- Design: Retrospective propensity score-matched cohort study.
- Setting: 51 health systems within the TriNetX US Collaborative Network
- Patients: Adults with T2D treated with either a GLP-1 receptor agonist or metformin between 2005 and 2024 who subsequently received an index diagnosis of MDS were identified.
- Matching: Two cohorts were defined – those treated with GLP-1RA (n=403) and patients treated with metformin (n=5,799). Patients were matched 1:1 using greedy nearest-neighbor propensity score matching.
- Outcomes: Progression to AML following MDS diagnosis analyzed using Kaplan-Meier curves and Cox proportional hazards models.

RESULTS

	Before PSM		After PSM		
Characteristic	GLP-1RA (n=403)	Metformin (n=5,799)	GLP-1RA (n=393)	Metformin (n=393)	SMD
Demographics					
Age, yrs (mean±SD)	69.2±10.8	73.0±10.2	69.5±10.7	69.1±11.8	
Male	50.1%	58.8%	50.4%	46.8%	0.071
Hispanic or Latino	6.2%	5.3%	5.9%	5.9%	<0.001
Black	16.4%	13.8%	16.5%	13.5%	0.086
Labs					
Platelets (×10 ³ /μL)	195±167	183±154	195±169	207±174	0.071
Hemoglobin (g/dL)	10.2±2.2	9.9±2.1	10.2±2.2	10.0±2.2	0.075
eGFR ≤60	58.1%	44.8%	57.5%	57.0%	0.010
BMI <30 kg/m ²	38.2%	49.9%	39.2%	38.7%	0.010
Neutrophils (×10 ³ /μL)	108±869	49.8±545	111±882	55.3±416	0.081
HbA1c (%)	6.6±1.5	6.7±1.4	6.6±1.5	6.5±1.5	0.041
Medications					
Insulin	57.6%	42.6%	57.3%	53.4%	0.077
Sulfonylurea	11.4%	17.0%	11.7%	10.9%	0.024
SGLT2 inhibitor	13.2%	6.3%	11.5%	9.4%	0.067
DPP-4 inhibitor	4.7%	9.3%	4.8%	3.3%	0.077
Diagnoses & Visits					
Hypertension	73.7%	68.1%	73.3%	69.2%	0.090
Ambulatory visit	89.3%	87.1%	89.1%	88.8%	0.008
Inpatient encounter	44.4%	41.7%	45.3%	42.0%	0.067



CONCLUSIONS

- Among patients with MDS and T2D, GLP-1RA exposure was associated with a significantly lower risk of progression to AML compared with metformin after accounting for demographic and clinical characteristics.
- These findings suggest that GLP-1RAs may influence leukemic progression in MDS and support further investigation into the biologic interplay between metabolic therapies and malignant hematopoiesis.
- Prospective studies are needed to validate these results.

REFERENCES

1. Ashruf OS, Hundal J, Mushtaq A, Kaelber DC, Anwer F, Singh A. Hematologic Cancers Among Patients With Type 2 Diabetes Prescribed GLP-1 Receptor Agonists. JAMA Netw Open. 2025;8(3):e250802. Published 2025 Mar 3. doi:10.1001/jamanetworkopen.2025.0802

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