Real-world Analysis on Impact of GLP-1 Receptor Agonists on All-Cause Mortality and Endocrine Therapy Tolerability in Breast Cancer Patients with Obesity

Colton Frisco Jones MD[1],Jonathan Gelfond PhD[2], Daisy Kwok BS[2], Elvis Obomanu MD[3], Stephanie Hadad DO[1], Yajur Arya MD[4], Arshi Syal MD[4], Virginia Kaklamani MD[1,5], Saba Shaikh MD[1,5]

[1]Division of Hematology/Oncology, University of Texas San Antonio, San Antonio, Texas; [2]Department of Population Health Sciences, University of Texas San Antonio, San Antonio, Texas; [3]Department of Medicine Jefferson Einstein Hospital, Philadelphia, Pennsylvania; [4]Department of Hematology/Oncology, Mayo Clinic-Jacksonville, Jacksonville, Florida; [5]University of Texas San Antonio Mays Cancer Center, San Antonio, Texas

Introduction

- Endocrine therapy (ET) improves survival in hormone receptor-positive breast cancer (BC).
- Obesity in patients with BC is associated with higher recurrence risk and worse survival.
- GLP-1 receptor agonists (GLP1RA) are used for the management of diabetes and obesity. Their impact on all-cause mortality and ET tolerability in patients with BC remains underexplored.
- This real-world analysis examines the effects of GLP1RA on these outcomes.

Methods

- De-identified data across 130 million patients, 108 health systems from the TriNetX database.
- Identified breast cancer patients, all stages, 18-90 years, with obesity (BMI ≥ 30), receiving endocrine therapy (ET).
- Grouped by GLP1RA exposure - receipt of at least 2 prescriptions.
- Primary endpoint: all-cause mortality.
- Secondary endpoint: ET tolerability - incidence of ET-related adverse effects.
- Propensity score matching performed by TriNetX adjusted for demographics, medical comorbidities, diabetes, stage, and prior chemotherapy. Multivariate logistic regression assessed associations.
- Subgroup analysis was performed for age (surrogate for menopause), Body Mass Index (BMI), type 2 diabetes status, ET type, and GLP1RA type.

Results

- After matching, a total of 17,568 participants were included in the study, with 8,784 assigned to each cohort **Figure 1**. Patient demographics and age at index event are highlighted in **Table 1**.
- Despite overall balance, slight imbalances persisted in hemoglobin A1c, BMI, and body weight.

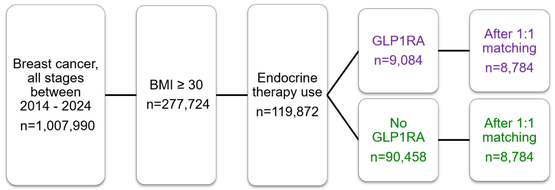


Figure 1. Flow Diagram for Patient Selection.

	GLP1RA (%) n=8784	No GLP1RA (%) n=8784	Standardized Mean Difference
Age at index event	58.4 (+/- 10.5 SD)	58.5 (+/- 11.6 SD)	0.012
White	6173 (70.3%)	6152 (70%)	0.005
Black	1528 (17.4%)	1,626 (18.5%)	0.029
Asian	203 (2.3%)	181 (2.1%)	0.017
Unknown Race	472 (5.4%)	419 (4.8%)	0.028
Female	8,701 (99.1%)	8,699 (99%)	0.003
Hemoglobin A1c	7.3 (+/- 1.7 SD)	6.4 (+/- 1.4 SD)	0.588
Body Mass Index	37.2 (+/- 7.1 SD)	34.3 (+/- 6.4 SD)	0.418

Table 1. Characteristics after Propensity Score Matching.

- GLP1RA use significantly reduced all-cause mortality **Figure 2**. The mean follow-up was 2,247 days for the GLP-1RA cohort and 2,093 days for the control. Mortality benefit was seen across subgroups **Figure 3**.

Results

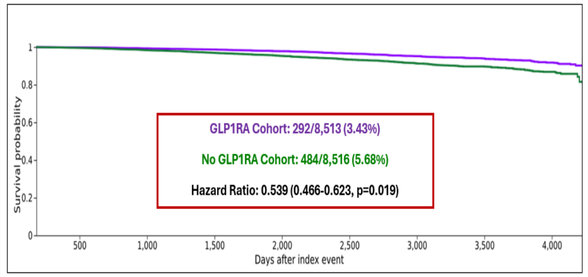


Figure 2. All-Cause Mortality.

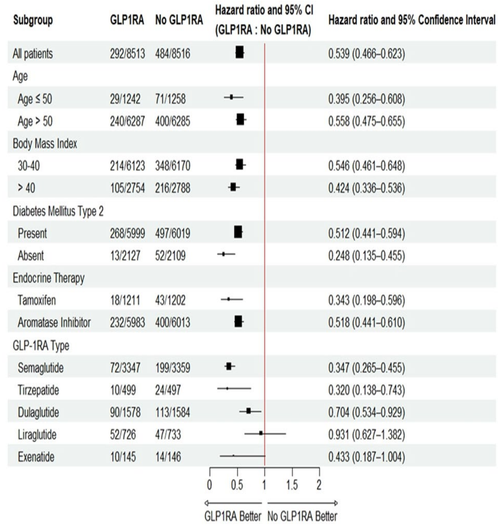


Figure 3. All-cause mortality for subgroups.

Results

- GLP1RA use significantly worsened joint pain, depression, hot flashes, osteoporosis, and endometrial cancer **Table 2**.
- Overall, there was not an increased risk of VTE. However, subgroup analysis revealed a significantly elevated risk in patients ≤ 50 years.

	GLP1RA cases/patients	No GLP1RA cases/patients	OR (95% CI)	p-value
Joint Pain	2,735/4,921 (56%)	2,092/5,260 (40%)	1.895 (1.751-2.050)	<0.0001
Depression	1,557/5,993 (30%)	1,049/6,514 (16%)	1.829 (1.675-1.996)	<0.0001
Hot Flashes	851/7,849 (11%)	638/7,957 (8%)	1.395 (1.253-1.554)	<0.0001
Osteoporosis	1,381/8,065 (17%)	1,152/7,938 (15%)	1.217 (1.118-1.325)	<0.0001
Endometrial Cancer	85/8,666 (1%)	53/8,679 (0.6%)	1.612 (1.143-2.275)	0.006
Venous Thromboembolism	594/8,185 (7%)	564/8,272 (7%)	1.069 (0.949-1.205)	0.271

Table 2. Endocrine Therapy Side Effects for Overall Cohort.

Conclusions

- This real-world analysis demonstrates that GLP-1RA use is associated with a significant reduction in all-cause mortality among BC patients with obesity undergoing ET.
- All-cause mortality benefit is seen across prespecified subgroups including age, BMI, Type 2 Diabetes Mellitus, and ET type.
- GLP-1 RA exposure appears to exacerbate several ET-related adverse effects.
- Future prospective studies are needed to determine these associations as they may warrant clinical consideration.

References

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