Impact of Glucagon-like peptide-1 receptor agonists Use on Survival and Metabolic Outcomes in Metastatic Estrogen Receptor Positive Breast Cancer: A Real-World Cohort Study

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Background

- Glucagon-like peptide-1 receptor agonists (GLP-1a), commonly used for type 2 diabetes and obesity, have shown potential anti-cancer effects in preclinical models.
- However, their impact on outcomes in patients with estrogen receptor-positive (ER+) metastatic breast cancer (MBC) remains unclear.
- This study evaluates the association between GLP-1a use and survival & metabolic outcomes in a real-world cohort of patients with ER+ MBC

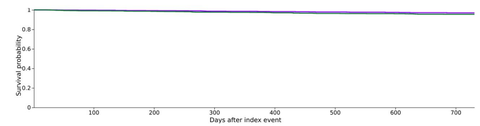
Objectives

- To evaluate the association between GLP-1 receptor agonist (GLP-1RA) use and survival and metabolic outcomes in patients with estrogen receptor–positive (ER+) metastatic breast cancer using real-world data.

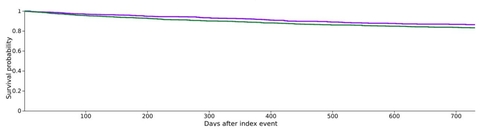
Methods

- We conducted a retrospective cohort study using the TriNetX US Collaborative Network. Two cohorts were defined:
- (1) ER+ MBC patients treated with GLP-1a (tirzepatide, dulaglutide, semaglutide, or liraglutide) and aromatase inhibitors (letrozole, anastrozole, or exemestane), excluding metformin users
- (2)ER+ MBC patients treated with aromatase inhibitors without GLP-1a or metformin.
- Cohorts were matched 1:1 using propensity scores based on demographics, comorbidities including type 2 diabetes mellitus and Obesity; and concurrent medications, including endocrine therapies and other systemic treatments such as CDK4/6 inhibitors, mTOR inhibitors, and HER2-targeted agents.
- Kaplan-Meier survival analyses were performed for overall survival and adverse outcomes over a 2-year follow-up.





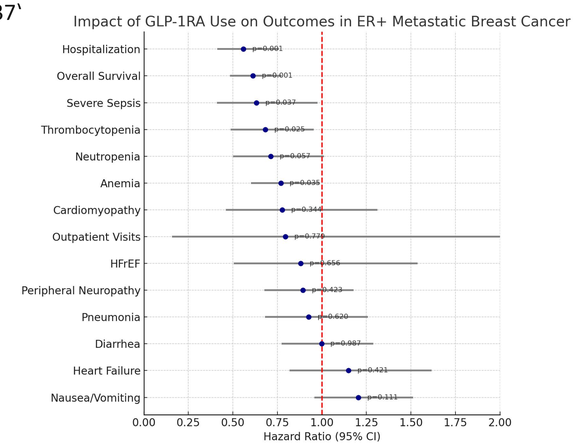
Severe Sepsis

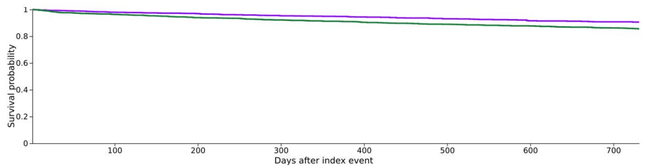


Anemia

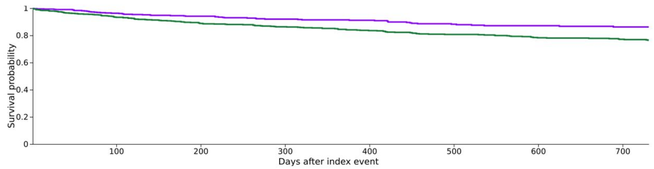
Results

- After propensity score matching, each cohort included 1,793 patients. GLP-1a use was associated with significantly improved 2-year overall survival (HR0.612, 95% CI: 0.484-0.773, p<0.001).
- Risk of hospitalization was also lower in the GLP-1a group (HR 0.559, 95% CI: 0.412-0.759, p<0.001).
- GLP-1a use was associated with reduced risk of Anemia (HR 0.769, 95% CI: 0.601-0.983, p=0.035), Thrombocytopenia (HR 0.682, 95% CI: 0.487-0.955,p=0.025) and Severe sepsis (HR 0.633, 95% CI: 0.411-0.975, p=0.037`





All-cause Mortality



Hospitalization

Results (continued)

- No significant differences were observed for Neutropenia (HR 0.712, 95% CI: 0.501-1.012, p=0.057), Nausea/vomiting (HR 1.204, 95% CI: 0.958-1.512,p=0.111), Outpatient visits (HR 0.795, 95% CI: 0.159-3.970, p=0.779), Heart failure (HR 1.150, 95% CI: 0.818-1.616, p=0.421), Cardiomyopathy (HR 0.777,95% CI: 0.460-1.312, p=0.344), Diarrhea (HR 0.998, 95% CI: 0.773-1.288, p=0.987), HFrEF (HR 0.881, 95% CI: 0.505-1.537, p=0.656), Pneumonia (HR 0.925,95% CI: 0.680-1.258, p=0.620), Peripheral neuropathy (HR 0.893, 95% CI: 0.677-1.178, p=0.423).

Conclusions

- This large retrospective cohort analysis provides evidence suggesting that GLP-1a use in patients with ER+ metastatic breast cancer may offer survival benefits beyond their established metabolic indications.
- The association between GLP-1a use and improved two-year overall survival, as well as reduced hospitalizations and lower incidence of several treatment-related adverse events, is clinically significant and suggests a possible dual role for GLP-1a in addressing both metabolic and oncologic challenges in this population.
- Importantly, GLP-1a therapy was not associated with increased gastrointestinal or cardiac toxicity, reinforcing its safety profile when used alongside standard endocrine and targeted cancer therapies.
- These findings align with emerging data that metabolic interventions can impact tumor biology and patient outcomes, and they highlight the value of a multidisciplinary approach that addresses both oncologic and comorbid metabolic conditions.
- Future prospective studies and randomized clinical trials are needed to validate these results and further elucidate the underlying biological mechanisms by which GLP-1a may exert anti-tumor effects in ER+ MBC.
- This study signifies the evolving landscape of cancer care, where holistic, patient-centered strategies are increasingly recognized as essential for optimal outcomes.

Limitations

- This retrospective real-world study cannot establish causality and may be affected by residual confounding despite propensity matching.
- Medication adherence and treatment duration were not verifiable. Coding inaccuracies and variable follow-up across centers may have influenced results.
- Biological factors and tumor genomics were not captured, limiting mechanistic interpretation

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