

GLP-1 Receptor Agonists Improve Immunotherapy Outcomes in NSCLC: a TriNetX Propensity-Matched Cohort Study

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Introduction

- Concurrent use of glucagon-like peptide-1 receptor agonists (GLP-1RAs) in overweight or obese patients receiving immune checkpoint inhibitor (ICI) therapy for non-small cell lung cancer (NSCLC) has been associated with improved survival.
- Preclinical evidence suggests that this effect is mediated by immune modulation of the tumor microenvironment.
- In this study we evaluated GLP-1RA and ICI use in NSCLC using a large multi-institutional database.

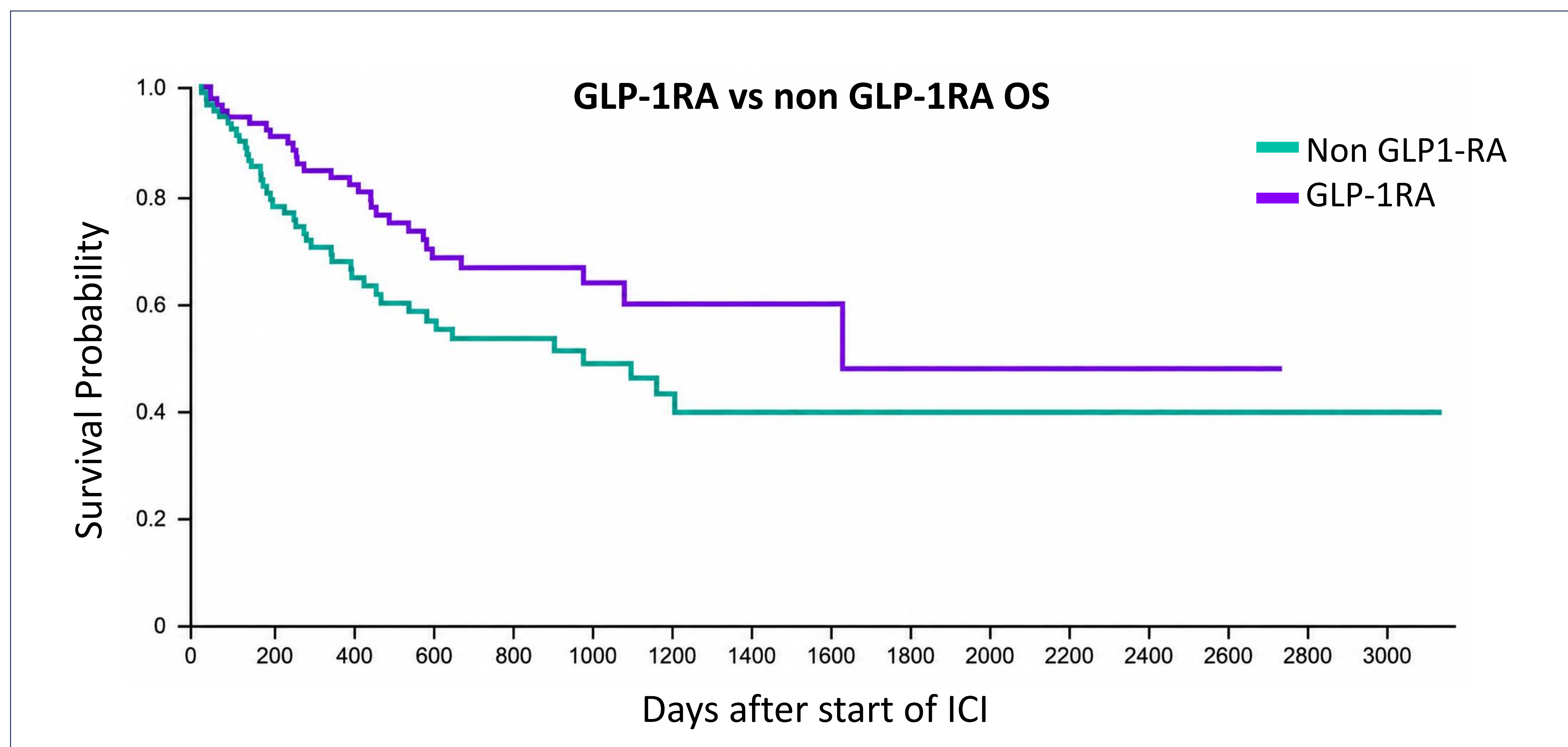
Methods

- We performed a retrospective cohort study using the TriNetX Global Collaborative Network.
- We identified adults with NSCLC treated with ICIs and body mass index (BMI) ≥ 25 . Cohorts were 1:1 propensity score matched based on demographics, tobacco use, ECOG (Eastern Cooperative Oncology Group) performance status, diabetes, obesity, cardiac disease, liver disease, chronic kidney disease, and other major comorbidities.
- We compared outcomes between patients who received GLP-1RAs within 1 year of beginning ICI therapy and those who did not (non GLP-1RA).
- The primary outcomes were overall survival (OS) and real-world progression-free survival (rwPFS), defined as time to second-line therapy or death.
- Survival was analyzed using the Kaplan-Meier method and cox proportional hazards regression.
- Secondary endpoints were immune-related adverse events (irAEs) and hospitalization rates and were evaluated by z-test.

Results

Outcomes	Non-GLP-1RA	GLP-1RA	Effect Estimate
Patients BMI ≥ 25 (n)	90	90	
Median OS (days)	976	1631	HR 0.604 (95% CI 0.37–0.97) p=0.038
Median rwPFS (days)	451	1079	HR 0.675 (95% CI 0.45–1.01) p=0.056
Patients all BMI (n)	142	142	
Median OS (days)	542	1359	HR 0.604 (95% CI 0.42–0.86) p=0.0048
Median rwPFS (days)	209	848	HR 0.587 (95% CI 0.43–0.80) p=0.0006

GLP-1RA use was associated with longer OS after treatment with ICI in this propensity matched real world cohort



Discussion

- Among 3134 eligible patients (3043 non-GLP-1RA, 91 GLP-1RA), 90 matched pairs were identified.
- Median follow-up was 702 days for non-GLP-1RA and 694 days for GLP-1RA patients.
- Median OS was significantly longer in patients treated with GLP-1RAs (976 vs 1631 days; Hazard Ratio [HR] 0.604, 95% CI 0.37 – 0.97; p=0.038).
- There was additionally a trend toward improved rwPFS for the GLP-1RA group (451 vs 1079 days; HR 0.675, 95% CI 0.45 – 1.01; p=0.056).
- GLP-1RAs were also associated with reduced risk of pulmonary irAE (18% vs 34% of patients; p=0.01), but no difference in hospitalizations (57% vs 61% of patients; p=0.87).
- In the sensitivity analysis including patients of all BMIs, the association remained significant for OS (542 vs 1359 days, HR 0.604, 95% CI 0.42 – 0.86; p=0.0048) and rwPFS (254 vs 848 days, HR 0.587, 95% CI 0.43 – 0.80; p=0.0006).

Limitations

- These exploratory findings are limited due to the observational study design and potential residual confounding.
- Further investigation into the effects of GLP-1RA medication on immunotherapy is needed.

References

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