10507 Oral Abstract Session

Glucagon-like peptide-1 receptor agonists and incidence of obesity-related cancer in adults with diabetes: A target-trial emulation study.

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Background: Obesity is a major risk factor for cancer development. However, whether glucagon-like peptide-1 receptor agonists (GLP-1RAs), a class of diabetes medication which causes weight loss, reduce cancer incidence is unknown. This study investigated whether GLP-1RAs reduce the risk of obesity-related cancer in adults with diabetes and obesity compared to dipeptidyl peptidase-4 inhibitors (DPP-4is), a weight-neutral class of diabetes medication. **Methods:** 85,015 adult patients from 43 U.S. health systems with a body mass index ≥ 30 kg/m2 and a diagnosis of diabetes, who newly initiated a GLP-1RA or DPP-4i between 2013 and 2023 were included. Patients prescribed GLP-1RAs (mean age, 56.8 years) were matched 1:1 on propensity score for GLP-1RA prescription and prescription year with patients prescribed DPP-4is (mean age, 56.8 years). Obesity-related cancer incidence was compared between groups. **Results:** Over a mean follow-up of 3.9 years, there was a lower risk of obesity-related cancers (adjusted HR, 0.93; 95% CI, 0.88-0.98; P=0.005) and all-cause death (adjusted HR, 0.92; 95% CI 0.87-0.97; P=0.001) associated with GLP-1RA use versus DPP-4i use. Assessments of cancer subtypes showed protective associations between GLP-1RA use and colon and rectal cancers. **Conclusions:** GLP-1RAs were associated with a lower risk of obesity-related cancer compared with DPP-4is in a large, real-world cohort of patients with diabetes and obesity. Future studies should prospectively assess the role of GLP-1RAs in cancer prevention. Research Sponsor: National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health; R01 DK115534 to MEG; National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health; K24 HL155861 to MEG; National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health; K01 DK121825 to JS.

Adjusted hazard ratios of incidence of composite obesity-related cancer and all-cause death in propensity-matched patients prescribed GLP-1RAs versus DPP-4is (n=85,015 pairs).

Outcome	Sex	Events/$N_{at\ risk}$ (GLP-1RA)	Events/$N_{at\ risk}$ (DPP-4i)	HR (GLP-1RA/ DPP-4i)	P	$P_{interaction}$
Obesity-related cancer (composite)	Overall	2,501/85,015 (2.9%)	2,671/85,015 (3.1%)	0.93; 95% CI, 0.88-0.98	0.005	NA
Obesity-related cancer (composite)	Female	1,754/44,762 (3.9%)	1,898/45,182 (4.2%)	0.92; 95% CI, 0.86-0.98	0.01	0.63
Obesity-related cancer (composite)	Male	747/40,253 (1.9%)	773/39,833 (1.9%)	0.95; 95% CI, 0.86-1.05	0.29	0.63
All-cause death	Overall	2,783/85,015 (3.3%)	2,961/85,015 (3.5%)	0.92; 95% CI, 0.87-0.97	0.001	NA
All-cause death	Female	1,219/44,762 (2.7%)	1,514/45,182 (3.4%)	0.80; 95% CI, 0.74-0.86	<0.001	<0.001
All-cause death	Male	1,564/40,253 (3.9%)	1,447/39,833 (3.6%)	1.04, 95% CI, 0.96-1.11	0.34	<0.001

Adjusted hazards ratios calculated using Cox regression represent ratios of the incidence of composite obesity-related cancer and all-cause death in matched pairs of patients prescribed GLP-1RA versus DPP-4i over average follow-up durations of 3.8 years (GLP-1RA) and 3.9 years (DPP-4i). Results of sex-stratified and sex interaction analyses are also displayed. The threshold for statistical significance is $P<0.05$.