10508 Oral Abstract Session

Association of glucagon-like peptide 1 receptor agonists with cancer risk in obesity adults with and without diabetes: A target trial emulation study.

Hao Dai, Yao An Lee, Ying Lu, Thomas J. George, Jingchuan Guo, Jiang Bian; Department of Health Outcomes and Biomedical Informatics, University of Florida, Gainesville, FL; Department of Pharmaceutical Outcomes and Policy, University of Florida, Gainesville, FL; University of Florida Health Cancer Center, Gainesville, FL; University of Florida, Gainesville, FL; Regenstrief Institute, Inc., Indianapolis, IN

Background: The use of glucagon-like peptide 1 receptor agonists (GLP-1RAs) has substantially expended given their remarkable benefits in managing obesity. Yet, their impact on long-term cancer risk remains unclear, with existing real-world evidence being limited and yielding conflicting results. **Methods:** This retrospective cohort study followed a target trial emulation design using 2014–2024 OneFlorida+ electronic health records (EHR) data. Adults (≥18 years) eligible for anti-obesity medications (AOMs) and without a cancer history were included. We compared GLP-RA users vs. non-users, with 1:1 propensity score matching applied to balance baseline factors between the two groups. The primary outcomes include the incidence of 16 obesity-associated cancers (liver, thyroid, pancreatic, bladder, colorectal, lung, kidney, breast, endometrial, meningioma, esophageal adenocarcinoma, gallbladder, upper stomach, ovarian, multiple myeloma, and prostate), assessed over a follow-up period of up to 10 years. Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs), and cumulative incidences were estimated using Kaplan-Meier analyses. **Results:** After matching, 43,317 GLP-1RA users were compared with 43,315 non-users. The incidence rates of the 16 cancers were 20.5 versus 23.6 per 1,000 person-years, respectively, indicating a significantly lower overall cancer risk among GLP-1RA users (HR, 0.83 [95% CI, 0.76–0.91]) compared to non-users. In particular, GLP-1RA use was associated with a reduced risk of endometrial cancer (HR, 0.75 [95% CI, 0.57–0.99]), ovarian cancer (HR, 0.53 [95% CI, 0.29–0.96]), meningioma (HR, 0.69 [95% CI, 0.48–0.97]), and esophageal adenocarcinoma (HR, 0.34 [95% CI, 0.12–0.94]). However, GLP-1RA users showed a trend toward an increased risk of kidney cancer (HR, 1.38 [95% CI, 0.99–1.93]), particularly among the younger adults (≤65 years) and overweight patients (BMI 27–29.9). **Conclusions:** In this large cohort of real-world obesity population with and without diabetes, GLP-1RA use was associated with an overall reduction in obesity-related cancer risk, as well as lower risks of several specific cancers. However, a potential elevated risk of kidney cancer, especially in younger or moderately obese individuals, highlights the need for targeted surveillance and longer-term follow-up to clarify the underlying mechanisms and clinical implications of these findings. Research Sponsor: None.