

GLP-1 receptor agonist and SGLT2 inhibitor use and weight change following androgen deprivation therapy initiation among men with prostate cancer

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Background: Androgen deprivation therapy (ADT) can lead to metabolic dysfunction including weight gain among patients with prostate cancer. GLP-1 receptor agonists (GLP-1 RAs) and SGLT2 inhibitors (SGLT2is) are emerging medication classes that have revolutionized glycemic control, with GLP-1 RAs showing stronger weight-loss effects than SGLT2is. We examined whether concurrent GLP-1 RA or SGLT2i use modifies weight change following ADT initiation in a multi-institutional database.

Methods: The TriNetX Linked Network database contains electronic health record and insurance claims data from patients at 44 U.S. healthcare organizations. Within TriNetX, we identified a cohort of patients with prostate cancer who had initiated use of a GLP-1 RA, SGLT2i, or DPP-4 inhibitor (DPP4i; as a metabolically neutral active comparator) between 2015-2025, with initiation preceding ADT (regardless of timing relative to prostate cancer diagnosis), and recorded weights both pre- and post-ADT initiation. Weight changes were evaluated from time of GLP-1 RA/SGLT2i/DPP-4i initiation (index date) until discontinuation, switch to a different study medication, or administrative censoring. Mean weight change per year (kg/year) was estimated using within-person linear-spline mixed effects models, with a knot at time of ADT initiation to allow for different pre- and post-ADT slopes. Models were adjusted for patient age, race and ethnicity, calendar year, disease extent, comorbid cardiometabolic conditions, and prior use of other anti-diabetic medications. Differences in post-ADT slopes across medication classes were evaluated using a likelihood ratio test.

Results: 565 patients (median age 67, IQR: 63-73 at index date) met eligibility criteria with 211 initiating a GLP-1 RA, 180 SGLT2i, and 174 DPP4i a median 188 days (IQR 70-447) prior to ADT initiation. Median weight at index date was 95kg (IQR 81-112kg). 35% of patients had metastatic prostate cancer and 77% of patients received an ADT agonist. In a separate analysis restricted to the 6 months following medication initiation (before ADT), GLP-1 RA use was associated with significant weight loss (mean -1.68 kg, $p < 0.001$), while DPP4i and SGLT2i were not ($p = 0.74$ and $p = 0.67$, respectively). Overall, weight was stable prior to ADT initiation (mean -0.24 kg/yr, 95%CI -0.81, 0.32) and ADT initiation was associated with a non-statistically significant 0.69 kg/yr mean increase in the rate of weight change (95%CI -2.13, 3.51). Rates of weight change across medication classes following ADT initiation differed, wherein patients using GLP-1 RAs continued to lose weight (-0.79 kg/yr, 95%CI -4.09, 2.50) while patients using SGLT2i (1.95 kg/yr, 95%CI -1.57, 5.46) and DPP4i (0.69 kg/yr, 95%CI -2.06, 3.44) gained weight.

Conclusions: In this analysis, the rate of ADT-associated weight gain was suggestively lower among patients using a GLP-1 RA, but not a SGLT2i, building on GLP-1 RA's independently-demonstrated weight-loss effect prior to ADT. As usage increases, prospective studies are needed to clarify GLP-1 RA's cardiometabolic effects during ADT.

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