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Incretin-Based Weight Loss Therapies: Weighing the Protective Potential Against Breast Cancer

Betül Keyif[1*], **Mertihan Kurdoğlu**[2], **Arash Khaki**[3]

Incretin-based treatments, which have gained fame as obesity drugs, are in the spotlight with their promise of rapid weight loss. But could this new generation of weight loss drugs also help reduce breast cancer risk?

Glucagon-like peptide-1 (GLP-1) receptor agonists (RAs), including semaglutide and liraglutide, together with the dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) agonist tirzepatide, were initially formulated for type 2 diabetes but have rapidly gained popularity as weight management agents, particularly for off-label cosmetic weight loss spurred by social media influence (1).

These incretin-based medications induce substantial weight reduction and metabolic changes by slowing gastric emptying, suppressing appetite, reducing glucagon release, and enhancing glucose-dependent insulin secretion (2, 3).

A clear pattern has emerged: despite the costs and uncertainties, the potential for swift weight loss has generated considerable excitement about these injections. Their emergence drew attention to potential oncologic benefits, considering that hormonal and metabolic dysregulation associated with obesity is a recognized breast cancer risk factor (4, 5). Excess adiposity in postmenopausal women increases breast cancer incidence and exacerbates prognosis, mainly due to heightened estrogen synthesis (via aromatase in adipose tissue) and hyperinsulinemia that facilitates tumor growth (2, 3). Intentional weight loss is linked to enhanced cancer outcomes; for instance, bariatric surgery in obese individuals is related to a markedly reduced breast cancer incidence (2).

It is proposed that pharmaceutical weight loss with GLP-1/GIP agonists might also reduce breast cancer incidence (2, 4). Current clinical results are reassuring regarding safety: comprehensive assessments have revealed no rise in breast neoplasm incidence among patients with GLP-1 RAs (6).

Emerging data support protective benefits. A substantial cohort of 1.1 million patients demonstrated a markedly diminished incidence of various malignancies among GLP-1 RA users, with roughly 28% fewer breast cancer cases relative to matched non-users (hazard ratio ~0.72) (7). Likewise, recent studies indicate that using GLP-1 RAs correlates with reduced incidence of certain obesity-related cancers (8).

Betül Keyif graduated from Uludağ University Faculty of Medicine in Bursa, Turkey. She completed her residency in obstetrics and gynecology at the İstanbul University Faculty of Medicine in 2016. Following her specialization, she served as an obstetrician and gynecologist at various state hospitals, including Hakkari Yüksekova State Hospital, Bolu İzzet Baysal Maternity & Children's Hospital, and Bursa Kestel State Hospital. Since 2021, she has worked as an Assistant Professor in the Department of Obstetrics and Gynecology at Düzce University Faculty of Medicine. Her clinical and academic interests include gynecological oncology, minimally invasive surgery, reproductive endocrinology, and polycystic ovary syndrome (PCOS).

However, these data are mainly observational and should be considered cautiously. Outcomes exhibit heterogeneity; for instance, semaglutide demonstrated significant reductions in cancer risk in one analysis, while liraglutide was related to an elevated thyroid tumor risk in the same study, highlighting the complexity of differentiating drug effects from underlying patient characteristics (7).

No prospective research has definitively demonstrated a causal decrease in breast cancer incidence linked to incretin-based therapy, and confounding factors, such as a healthier lifestyle among those using the drug, cannot be ruled out. Consequently, although GLP-1/GIP agonists improve significant risk factors (obesity, hyperinsulinemia) and initial data appear promising, it is still premature to regard them as an obvious preventive against breast cancer (3, 8).

Further large-scale studies will elucidate whether these drugs possess a cancer-preventive function. Incretin-based therapies show promise for metabolic health and possibly cancer risk reduction, but it is too early to consider them a reliable shield against breast cancer.

Authors' Contribution

Conceptualization: Mertihan Kurdoğlu.
Project administration: Mertihan Kurdoğlu.
Supervision: Mertihan Kurdoğlu.

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[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Düzce University, Düzce, Türkiye. [2]Department of Obstetrics and Gynecology, Faculty of Medicine, Gazi University, Ankara, Türkiye. [3]Department of Pathology, TMS.C, Islamic Azad University, Tabriz, Iran.
*Corresponding Author: Betül Keyif, Email: betul_keyif@hotmail.com

Writing–original draft: Betül Keyif and Mertihan Kurdoğlu.
Writing–review & editing: Mertihan Kurdoğlu, Arash Khaki.

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