COMMENT ON BEZIN ET AL.

GLP-1 Receptor Agonists and the Risk of Thyroid Cancer. Diabetes Care 2023;46:384–390

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We read the article by Bezin et al. (1) with interest and would like to point out several flaws that make the interpretation unreliable.

The control group has 9.6% of individuals treated with a glucagon-like peptide receptor agonist (GLP-1 RA) for various durations, thereby making it difficult to suggest causality. Instead, an ideal comparison would be to look at incidence of thyroid cancer in those on a GLP-1 RA versus those not on a GLP-1 RA and a third arm to compare with the incidence of thyroid cancers in individuals without diabetes and not on a GLP-1 RA.

There is no exclusion of thyroid nodules/cancer prior to initiation on GLP-1 RA therapy, and therefore it is unknown if these individuals already had thyroid cancer. The most common type of thyroid cancer (papillary thyroid carcinoma) is extremely slow growing, with tumor doubling time $\geq$5 years (2). Furthermore, the duration of exposure to a GLP-1 RA was too short to cause drug-induced cancer development per current evidence (3).

Medullary thyroid cancer in this study formed 15.5% of all cases (compared with $<$3% seen in the literature [4]), suggesting that methods used by the authors to assume medullary thyroid cancer are too simplistic, leading to gross overestimation. As the authors do not mention whether calcitonin levels were elevated or not, these data are not really suggestive of thyroid cancer. Patients with thyroid cancer on a GLP-1 RA are probably more likely to get calcitonin levels checked, reflecting testing bias.

Hence, we recommend that the conclusions suggested by this article are at best hypothesis generating, especially when a recent meta-analysis demonstrated a neutral effect for GLP-1 RAs and thyroid cancer (5).

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