Diabetes therapy and cancer risk: Where do we stand when treating patients?

ABSTRACT

The pathophysiology of type 2 diabetes mellitus conveys increased cancer risk, and any antidiabetic drug may alter that risk in a favorable or unfavorable way. This article discusses the links between diabetes and cancer, the different agents available for treating diabetes, and the cancer risk associated with these therapies.

KEY POINTS

- Exogenous insulin, insulin secretagogues, and incretin-based therapies are under scrutiny because of their potential influences on cancer development in a population already at risk.

- At present, we lack adequate prospective data on the cancer risk from diabetes drugs.

- Patients with a personal history of bladder cancer should avoid pioglitazone, and those who have had pancreatic cancer should avoid incretin therapies until definitive clinical data become available.

- Patients with a personal or family history of medullary thyroid cancer or multiple endocrine neoplasia type 2 should not receive glucagon-like peptide-1 receptor agonists. These agents should also probably be avoided in patients with a personal history of differentiated thyroid carcinoma or a history of familial nonmedullary thyroid carcinoma.

- Given the associations between diabetes and malignancy, cancer screening is especially important.

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IN THE LAST QUARTER CENTURY, many new drugs have become available for treating type 2 diabetes mellitus. The American Association of Clinical Endocrinologists incorporated these new agents in its updated glycemic control algorithm in 2013.1 Because diabetes affects 25.8 million Americans and can lead to blindness, renal failure, cardiovascular disease, and amputation, agents that help us treat it more effectively are valuable.2

One of the barriers to effective treatment is the side effects of the agents. Because some of these drugs have been in use for only a short time, concerns of potential adverse effects have arisen. Cancer is one such concern, especially since type 2 diabetes mellitus by itself increases the risk of cancer by 20% to 50% compared with no diabetes.3

Type 2 diabetes has been linked to risk of cancers of the pancreas,4 colorectum,5,6 liver,7 kidney,8,9 breast,10 bladder,11 and endometrium,12 as well as to hematologic malignancies such as non-Hodgkin lymphoma.13 The risk of bladder cancer appears to depend on how long the patient has had type 2 diabetes. Newton et al.,14 in a prospective cohort study, found that those who had diabetes for more than 15 years and used insulin had the highest risk of bladder cancer. On the other hand, the risk of prostate cancer is actually lower in people with diabetes,15 particularly in those who have had diabetes for longer than 4 years.16

Cancer and type 2 diabetes share many risk factors and underlying pathophysiologic mechanisms. Nonmodifiable risk factors for both diseases include advanced age, male