Metformin May Cut Risk of Cancer in Type 2 Diabetes

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Contributing Writer

GLASGOW, SCOTLAND — Metformin may protect against the development of cancer in patients with type 2 diabetes, according to findings from a large cohort study.

Among patients with diabetes who had been treated with metformin, 7.9% developed cancer, compared with 12.9% of diabetics who had never used the drug, reported Dr. Josie Evans of the University of Dundee (Scotland).

"Since the publication of the United Kingdom Prospective Diabetes Study (UKPDS), metformin is now one of the most commonly used oral antidiabetic medications in the world," Dr. Evans said at the annual professional conference of Diabetes U.K.

Interest in an association between metformin and the development of cancer stems from the observation that the oral antidiabetic agent acts via the enzyme AMP-activated protein kinase, which is affected by the presence of LKB1, a well-known tumor suppressor. Previous research by Dr. Evans and her associates showed that of 3,828 patients with type 2 diabetes receiving hospital treatment for cancer, 1,276 had used metformin and 2,552 had not (BMJ 2005;330:1304-5).

Building on these pilot study data, the researchers performed a larger cohort study involving 8,170 patients diagnosed with type 2 diabetes, 4,085 of whom had been treated with metformin.

"When we excluded people who had only received one prescription of metformin, we still found a big difference in the proportions of users and nonusers who developed cancer," Dr. Evans said. The cancer rate was 7.3% in patients who had used metformin more than once and 11.9% in those who had never used the antidiabetic drug.

"Of course one of the problems with this study is that it is an observational study, and it may be that the metformin users were at lower baseline risk of cancer than the comparators," she commented.

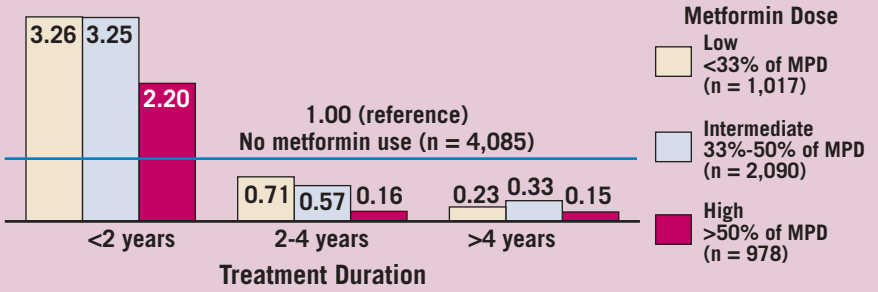
One of the most significant differences in the patients at baseline was that the metformin users were an average of 6 years younger than the nonusers. But after adjusting for age, smoking history, and body mass index, among other variables, outcomes remained in favor of metformin use. Similar results were obtained for other outcomes, including all-cause mortality and mortality from cancer, as well as the incidence of three common cancers—colorectal, breast, and lung.

"We wanted to be sure that it's the metformin that is associated with a reduced risk of cancer and not something to do with people who are taking metformin," Dr. Evans said, "so we looked to see if we could find a dose effect associated with metformin." Although the data initially seemed to show a dose effect, this appeared to be confounded by the duration of treatment. Nevertheless, stratifying the results by dose and by duration suggested that there is "some evidence of a dose effect of metformin." (See box.)

Dr. David Matthews of the Oxford (England) Center of Diabetes, Endocrinology and Metabolism commented that there was no evidence that the cardiovascular protection afforded by metformin in the UKPDS was dose related, so perhaps the same will hold true for metformin and cancer.

The study was supported by Tenovus Scotland, a charitable organization. ■

Adjusted Hazard Ratios for Development of Cancer In Patients With Type 2 Diabetes



Notes: Hazard ratios were adjusted for factors including age, smoking history, and body mass index. MPD is maximum prescribable dose.
Source: Dr. Evans

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