

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.

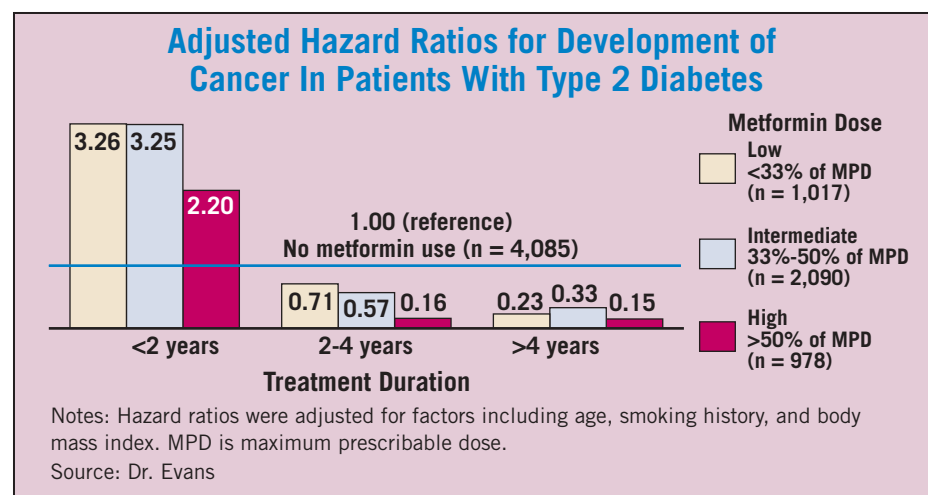
“Of course one of the problems with this study is that it is an observational study, and it may be that the metformin users were at lower baseline risk of cancer than the comparators,” she commented.

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. ■



Norditropin® Indications and Usage

Norditropin® (somatropin [rDNA origin] injection) is indicated for the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone, the treatment of children with short stature associated with Noonan syndrome and Turner syndrome, and for the replacement of endogenous growth hormone in adults with growth hormone deficiency (GHD) who meet either of the following two criteria: 1. Adult Onset: Patients who have GHD, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma; or 2. Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.

Important Safety Information

Somatropin should not be used for growth promotion in pediatric patients with closed epiphyses or in patients with active proliferative or severe non-proliferative diabetic retinopathy. Norditropin should not be used in patients with known hypersensitivity to somatropin or any of its excipients.

Somatropin should not be used or should be discontinued with any evidence of active malignancy. Patients with preexisting malignancy should be monitored carefully for any progression or reoccurrence.

Somatropin should not be used to treat patients with acute critical illness due to complications following open heart or abdominal surgery, multiple accidental trauma or acute respiratory failure as increased mortality may occur.

Deaths have been reported in patients with Prader-Willi syndrome who are severely obese or have severe respiratory impairment and are treated with somatropin. Unless patients with Prader-Willi syndrome also have a diagnosis of GHD, Norditropin is not indicated for the treatment of patients who have growth failure due to genetically confirmed Prader-Willi syndrome.

Blood glucose levels should be monitored periodically as treatment with somatropin may decrease insulin sensitivity. Patients with preexisting diabetes or glucose intolerance should be monitored closely during somatropin therapy. Doses of insulin or oral agents may need to be adjusted for patients with diabetes on somatropin therapy.

Intracranial hypertension (IH) with papilledema, visual changes, headache, nausea and/or vomiting has been reported in a small number of patients treated with somatropin products. Symptoms usually occurred within the first eight (8) weeks after initiation of somatropin therapy and generally resolve after cessation of therapy or a reduction of the somatropin dose. Funduscopic examination should be performed routinely before initiating and periodically during the course of somatropin therapy. If papilledema is observed by funduscopy during somatropin treatment, treatment should be discontinued.

Pediatric patients may develop slipped capital femoral epiphyses more frequently if they have endocrine disorders or during rapid growth. Any child having onset of a limp or complaints of hip or knee pain during somatropin therapy should be carefully evaluated. Progression of scoliosis can occur in patients who experience rapid growth. Somatropin has not been shown to increase the occurrence of scoliosis.

In patients with GHD, central (secondary) hypothyroidism may first become evident or worsen during somatropin treatment. Patients treated with somatropin should therefore have periodic thyroid function tests and thyroid hormone replacement therapy should be initiated or adjusted as needed.

Patients with Turner syndrome should be evaluated carefully for otitis media and other ear disorders since these patients have an increased risk of ear and hearing disorders. Somatropin treatment may increase the occurrence of otitis media in patients with Turner syndrome. In addition, patients with Turner syndrome should be monitored closely for cardiovascular disorders (e.g., stroke, aortic aneurysm/dissection, hypertension) as these patients are also at risk for these conditions.

Although from a clinical study in Noonan syndrome there was no evidence of somatropin-induced ventricular hypertrophy or exacerbation of preexisting ventricular hypertrophy (as judged by echocardiography), the safety of Norditropin in children with Noonan syndrome and significant cardiac disease is not known.

Somatropin inhibits 11 β -hydroxysteroid dehydrogenase type 1 (11 β HSD-1) in adipose/hepatic tissue, and may significantly impact the metabolism of cortisol and cortisone. In patients treated with somatropin, previously undiagnosed central (secondary) hypoadrenalism may be unmasked requiring glucocorticoid replacement therapy. In addition, patients treated with glucocorticoid replacement therapy especially with cortisone acetate and prednisone for previously diagnosed hypoadrenalism may require an increase in their maintenance or stress doses.

Careful monitoring is advisable when somatropin is administered in combination with other drugs known to be metabolized by CP450 liver enzymes (e.g., corticosteroids, sex steroids, anticonvulsants, cyclosporine) or other hormone replacement therapy.

The safety and effectiveness of Norditropin in patients age 65 years and older has not been evaluated in clinical studies. Elderly patients may be more sensitive to the actions of somatropin and may be more prone to develop adverse reactions.

Common somatropin-related adverse reactions include injection site reactions/rashes, lipatrophy and headaches, glucose intolerance, fluid retention and unmasking of latent central hypothyroidism.

Most serious adverse reactions reported for somatropin include intracranial hypertension, diabetic retinopathy, glucose intolerance, slipped capital femoral epiphysis, progression of preexisting scoliosis, sudden death in pediatric patients with Prader-Willi syndrome with risk factors including severe obesity, history of upper airway obstruction or sleep apnea and unidentified respiratory infection, and intracranial tumors as a 2nd tumor in patients who had been treated for a 1st neoplasm.

Please see brief summary of Prescribing Information on following page.

Reference: 1. Norditropin® cartridges [prescribing information]. Princeton, NJ: Novo Nordisk Inc; September 2007.

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