Sulfonylureas Tied to Mortality in MI Survivors

BY BRUCE JANCIN

BARCELONA — Four widely prescribed oral sulfonylurea drugs are associated with significantly increased risk of all-cause mortality compared with metformin in type 2 diabetic patients having a history of MI, according to a comprehensive Danish national cohort study.

The study included all Danish adults with a prior MI who started on oral glucose-lowering monotherapy during 1997-2006. The conclusion: Glimepiride, glyburide, glipizide, and tolbutamide were associated with 33%-43% higher mortality risk than was metformin, Dr. Tina Ken Schramm said at the annual congress of the European Society of Cardiology.

In contrast, single-agent gliclazide and repaglinide had all-cause mortality risks similar to metformin.

"The clinical implication of this is that metformin, gliclazide, and repaglinide appear superior to other single-drug treatments received. We believe that metformin in general should be part of the treatment of type 2 diabetes to reduce mortality, but gliclazide and repaglinide may be good alternatives," said Dr. Schramm of the Heart Center at Copenhagen University National Hospital.

Metformin deserves the nod as the first-line agent on the basis of the results of the landmark United Kingdom Prospective Diabetes Study, which convincingly established the drug as the safest glucose-lowering agent available.

Out of the total Danish population of roughly 4.1 million, 107,870 type 2 diabetic individuals initiated monotherapy with a glucose-lowering agent during the 9-year study period. Among them were 9,135 with a prior MI, who formed the population for this study.

Glimepiride was the most widely prescribed of the glucose-lowering medications in Denmark, being used by 43% of subjects. Next came metformin (32%), glyburide (13%), glipizide and gliclazide (7% each), tolbutamide (6%), and repaglinide (2%). Acarbose was prescribed

Glimepiride, glyburide, glipizide, and tolbutamide were associated with higher mortality than metformin.

DR. SCHRAMM

as monotherapy in only 44 patients nationwide—far too small a number to allow meaningful results. Similarly, the thiazolidinediones, which in Denmark are not recommended therapy in this clinical setting, were used too seldom to draw any conclusions, explained Dr. Schramm, who reported having no financial conflicts of interest regarding the study.

Metformin served as the comparator in determining all-cause mortality risks for the other oral glucose-lowering agents in a multivariate analysis adjusted for age, gender, years of diabetes, cardiovascular medications, and socioeconomic status.

Audience members asked if confounding was a potential issue in the study—that is, perhaps patients on drugs other than metformin were sicker, or had previously been on metformin but proved intolerant or unresponsive to it. Dr. Schramm replied that it's unlikely, since when she performed a subanalysis restricted to those patients starting their first-ever glucose-lowering agent the results were unchanged.

She undertook the study because most prior trials oral glucose-lowering medications did not look beyond glucose-lowering efficacy in terms of outcomes. ■