COMMENTS AND RESPONSES

Medical Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy: A Consensus Statement of the American Diabetes Association and the European Association for the Study of Diabetes

Response to Nathan et al.

GlaxoSmithKline regrets the recommendation (1) of the recent American Diabetes Association/European Association for the Study of Diabetes consensus statement against the use of rosiglitazone for treatment of type 2 diabetes because it is contrary to scientific evidence.

The evidence regarding a possible association of rosiglitazone with increased risk of cardiovascular ischemic morbidity remains inconclusive. Data from clinical trials assessing cardiovascular outcomes are inconsistent with the hypotheses of increases in myocardial ischemia or death that have arisen from meta-analyses. No long-term clinical trials have confirmed an increased cardiovascular ischemic risk with rosiglitazone. Moreover, data from two large head-to-head clinical trials—A Diabetes Outcome Progression Trial (ADOPT) (2) and the interim report of Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycaemia in Diabetes (RECORD) (3)—show that, apart from the well-documented risk of heart failure with thiazolidinediones, rosiglitazone has a cardiovascular risk profile comparable with that of the recommended tier 1 antidiabetes medications, metformin and sulfonylureas.

The consensus statement contains multiple unexplained inconsistencies regarding the evidence underlying its conclusions and recommendations. Data from long-term clinical trials, which provide gold-standard evidence, sometimes appear to receive less weight than conclusions from hypothesis-generating meta-analyses. This circumstance is difficult to understand, particularly in light of a recent statement (4) by the corresponding author that "the vagaries of meta-analyses make them unreliable."

Furthermore, the consensus statement cites data in an inconsistent manner. Meta-analyses critical of rosiglitazone are mentioned repeatedly, while analyses reporting no increase in cardiovascular ischemic risk with rosiglitazone versus other established antidiabetes medications, such as those performed by Lago et al. (5) and the U.S. Food and Drug Administration (6), are overlooked. A meta-analysis (7) that reported a statistically significant increase in a composite end point of cardiovascular hospitalization or mortality with the combination of sulfonylureas and metformin, a tier 1 recommended option, is not mentioned in the consensus statement.

Nathan et al. (1) state that "the overarching principle in selecting a particular intervention will be its ability to achieve and maintain glycemic goals." Rosiglitazone has been shown to provide glycemic control for up to 5 years—significantly longer than the most commonly used oral antidiabetes medications, sulfonylureas and metformin (2). GlaxoSmithKline strongly believes that rosiglitazone has a place in the therapeutic armamentarium for type 2 diabetes when used appropriately. Major regulatory agencies, including the U.S. Food and Drug Administration and the European Medicines Agency, have thoroughly reviewed all available safety and efficacy data for rosiglitazone in recent months and maintained the availability of rosiglitazone to patients.

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DOI: 10.2337/dc09-0125

Acknowledgments— A.R.C. and P.A. are employed by GlaxoSmithKline, manufacturer of rosiglitazone, and hold stock in the company. No other potential conflicts of interest relevant to this article were reported.

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