Triple Therapy in Type 2 Diabetes: Insulin Glargine or Rosiglitazone Added to Combination Therapy of Sulfonylurea Plus Metformin in Insulin-Naïve Patients

Response to Hamid and Simmons

Drs. Hamid and Simmons (1) comment on two positive aspects that favor the use of insulin glargine over rosiglitazone as add-on therapy in type 2 diabetic patients who are inadequately controlled on sulfonylurea plus metformin therapy. The first is whether the beneficial lipid effects found with insulin glargine versus rosiglitazone translate to better clinical outcomes. The second is in regard to the assessment of the cost profile associated with glargine.

The neutral effect on LDL levels of 1.4% with insulin glargine when compared with a 13.1% increase with rosiglitazone in type 2 diabetic patients provided significant differences between both interventions. Also, the reduction in triglyceride levels of 19% with insulin glargine is compared with a 4.6% increase with rosiglitazone. Although the relative cardiovascular impact of such modest LDL changes is not clear, the overall goal is to achieve the lowest LDL possible. Hamid and Simmons suggest that the increase in LDL levels with rosiglitazone may not be clinically detrimental since this may reflect an increase in larger, less atherogenic LDL particles that have been reported with thiazolidinediones. This may turn out to be true. However, recent National Cholesterol Education Program guidelines consider diabetes a coronary heart disease risk equivalent and indicate a treatment goal of LDL <100 mg/dl without qualifying particle size (2). Furthermore, LDL decreases have been linked to better cardiovascular outcomes in type 2 diabetic patients, and independent implications of changes in LDL particle size in this patient population are not clear (3,4).

A large (n = 12,612) ongoing cardiovascular outcomes trial (ORIGIN [Outcome Reduction With Initial Glargine Intervention]) (5,6) will assess whether insulin glargine can reduce cardiovascular risk in people with early dysglycemia; lipid levels will be assessed in conjunction with the primary end point of cardiovascular outcomes.

With regard to cost, the $70 price cited by Hamid and Simmons represents average retail cost, which is higher than the more uniform average wholesale price that is commonly used for comparative cost analysis. In our analysis (7), costs of both rosiglitazone and insulin glargine were based on actual study medication usage by all patients during the trial; average wholesale price for insulin glargine was $46.99 (8) at the time of the study analysis, resulting in actual cost of $216.00 per patient, as reported.

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An Open, Randomized, Parallel-Group Study to Compare the Efficacy and Safety Profile of Inhaled Human Insulin (Exubera) With Metformin as Adjunctive Therapy in Patients With Type 2 Diabetes Poorly Controlled on a Sulfonylurea

Response to Barnett et al.

We have several comments on the study of Barnett et al. (1) regarding the addition of premeal inhaled human insulin (INH) versus metformin as adjunctive therapy in patients with type 2 diabetes failing sulfonylureas.

First, the authors mentioned that decreases in 2-h postprandial glucose at week 24 in the INH and metformin groups were similar. However, inspection of data in Table 1 revealed that reduction of 2-h postprandial hyperglycemia was more pronounced in the INH group compared with the metformin group (75 and 59 mg/dl, respectively) (1). The difference between the adjusted mean change in 2-h postprandial hyperglycemia was −11.4 mg/dl with a 95% CI of −18.6 to −4.19 mg/dl (i.e. a CI that did not include zero). We believe this difference