COMMENTS AND RESPONSES

Response to Comment on: Bergenstal et al. A Randomized, Controlled Study of Once-Daily LY2605541, a Novel Long-Acting Basal Insulin, Versus Insulin Glargine in Basal Insulin–Treated Patients With Type 2 Diabetes. Diabetes Care 2012;35:2140–2147

We thank Professor Home for his interest (1) in our publication on a novel basal insulin analog, LY2605541 (2).

Total, LDL, and HDL cholesterol levels along with triglyceride levels (or lipid profiles) were measured as noted in the last paragraph on page 2144 (2). Whereas the serum triglyceride measurements for the LY2605541-treated patients did not differ from baseline but were higher compared with insulin glargine–treated patients, the total, HDL, and LDL cholesterol did not differ from baseline for the LY2605541-treated patients and did not differ from those treated with insulin glargine. In contrast, in the recently published type 1 diabetes study (3), LY2605541-treated patients demonstrated a modest increase in triglycerides and LDL cholesterol compared with baseline and to insulin glargine-treated patients, whereas the HDL cholesterol with LY2605541 decreased from baseline and compared with insulin glargine. As these findings were first noted in these exploratory phase 2 studies, the phase 3 studies will measure routine lipids and hepatic transaminase levels at frequent intervals to characterize the chronology of these changes. Additionally, in a subset of patients, these studies will measure hepatic fat content by magnetic resonance imaging, plasma lipoprotein subclass particle concentration (nmol/L), and particle size measured by nuclear magnetic resonance, total cholesterol efflux capacity, free fatty acids, cholesterylester transfer protein activity and mass, adiponectin, and apolipoproteins (Apo-A1, Apo-A2, Apo-B100, and Apo-CIII). Although high-sensitivity C-reactive protein would provide some information regarding inflammation, the determination of hepatic fat content was considered to be a fundamental investigation. The subsequent effects on insulin sensitivity along with determining inflammation were considered to be secondary. Lastly, because these patients were treated with exogenous insulin prestudy, and circulating levels of LY2605541 (similar to insulin detemir) are very different than that of human insulin, we question the validity of the homeostasis model assessment calculations under these circumstances.

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