

Effect of Rosiglitazone Treatment on Nontraditional Markers of Cardiovascular Disease in Patients With Type 2 Diabetes Mellitus

To the Editor:

In response to the article by Haffner et al,¹ I have the following comments. There were no inclusion or exclusion criteria cited within the article. How was it ethical to stop antidiabetic medications in patients for 4 weeks? In Table 1, there is no mention of other disease states or medications that may have affected the inflammatory state of the patients. I would also argue that the baseline HbA1c level is not an accurate reflection, because it looks at control for the previous 3 months, 4 weeks of which the subjects were taking no medications. The high-density lipoprotein and low-density lipoprotein cholesterol levels of 1.1, 3.0, 3.1, and 3.2 do not make sense, as they are labeled in mg/dL and there is no explanation as to where these numbers came from.

In the Figure, there is a different number of subjects in each graph for each group. The numbers are different from the study population of 357 at baseline randomization (95 in the placebo group, 126 in the rosiglitazone 4 mg group, and 136 in the rosiglitazone 8 mg group). Why were the other patients excluded? The authors also state on this page that “multivariate analyses of the change from weeks 0 to 26 also illustrated that the strongest correlates of change were between CRP, MMP-9, WBC, and IL-6 (data not shown)”;

 however, if these are the strongest data, why did they not show them? Another statement is made on page 683, saying “additionally, WBC has been shown to predict CVD,” and reference number 6 is cited. However, this reference focuses on C-reactive protein, not white blood cells.

I am also concerned that 136 subjects were not accounted for from the original number of subjects and there is no reason given. It was mentioned that the results for these subjects did not alter the results of the study; if so, why were they not included?

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1. Haffner SM, Greenberg AS, Weston WM, et al. Effect of rosiglitazone treatment on nontraditional markers of cardiovascular disease in patients with type 2 diabetes mellitus. *Circulation*. 2002;106:679–684.

Response

We would like to thank Jennifer Tuepker for her interest in our paper.¹ Our paper describes the results of additional analyses performed on subjects completing a 26-week study of rosiglitazone safety and efficacy. For questions regarding the design of this study, baseline values, and disposition of subjects, we refer Ms Tuepker to the paper describing the overall study by Lebovitz et al.² Readers should note that the study was approved by the Institutional Review Board at each site and all subjects gave informed consent.

Ms Tuepker points out correctly that the baseline lipid values presented in Table 1 do not make sense in terms of the units given for these values. Early versions of the manuscript presented these values in terms of traditional units (that is, mg/dL). The version submitted for publication showed these parameter values in SI units (that is, mmol/L); unfortunately, the reporting units in the table were not changed to reflect this. The values shown in the table are correct in terms of SI units. We intend to issue a correction to resolve this error.

With regard to the patient numbers shown in the Figure, these reflect subjects with paired baseline and week-26 values for the parameters being shown. There were 365 subjects who completed the study as scheduled, 357 of whom had paired values for at least 1 of the parameters shown. We realize that focusing our analysis on subjects who completed the study may have biased our conclusions, which was our motivation for performing a secondary analysis using the study intent-to-treat population, assuming no changes from baseline for patients with missing values (baseline values assumed to be equal to the mean for each treatment group). As stated in the paper, this secondary analysis is inherently more conservative; however, it yielded results similar to those of the primary analysis.

Ms Tuepker questioned our statement regarding multivariate analyses and correlates of change. This statement refers to additional analyses performed on these data that were left out of the final article because of space considerations.

Finally, Ms Tuepker suggests that we used an inappropriate reference citation to support the statement that white blood cell count has been shown to be predictive of cardiovascular disease. The correct citation for this statement should have been reference 16 rather than reference 6.

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1. Haffner SM, Greenberg AS, Weston WM, et al. Effect of rosiglitazone treatment on nontraditional markers of cardiovascular disease in patients with type 2 diabetes mellitus. *Circulation*. 2002;106:679–684.
2. Lebovitz HE, Dole JF, Patwardhan R, et al. Rosiglitazone monotherapy is effective in patients with type 2 diabetes. *J Clin Endocrinol Metab*. 2001;86:280–288.

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