

## COMMENTS AND RESPONSES

### Clinical Implications of the DREAM Study

Response to Davidson

The following points should be taken into consideration when determining “what circumstances TZDs [thiazolidinediones] should be used in people without documented diabetes,” as questioned by the commentary published in the February issue of *Diabetes Care* (1).

The DREAM (Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication) study (2) has limitations that prevent generalizations for individuals with impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT). In this study, individuals with IFG ( $n = 739$ ), IGT ( $n = 3,028$ ), or both ( $n = 1,502$ ) were included (3), and patient recruitment was completed between July 2001 and August 2003. Because these dates are earlier than November 2003 (4), when the American Diabetes Association accepted IFG as  $\geq 100$  mg/dl (5.6 mmol/l) and  $< 126$  mg/dl (7.0 mmol/l), individuals with glucose levels of  $\geq 6.1$  mmol/l

(110 mg/dl) and  $< 7.0$  mmol/l (126 mg/dl) were included in the study. Since the inclusion criteria (3) for the DREAM study included a fasting plasma glucose concentration  $\geq 6.1$  mmol/l, this affects both the selection of glucose-loaded patients as well as the patients who were included in the study as IFG in terms of increased risk of development of diabetes, as there is an inverted U-shaped curve relationship between fasting blood glucose level and mean plasma insulin concentration, also called Starling’s curve of the pancreas. Glucose-stimulated insulin response begins to decline at a fasting glucose concentration of  $\sim 110$ – $120$  mg/dl as a sign of failing of compensatory insulin response (5). Subsequently, the effectiveness of rosiglitazone in this group (6.1 mmol/l  $\leq$  IFG  $< 7$  mmol/l), which has already been approved for the treatment of diabetes, is an expected result. However, one cannot assume that rosiglitazone will be more affective than placebo in groups that have low risk of developing diabetes (5.6 mmol/l  $\leq$  IFG  $< 6.1$  mmol/l).

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DOI: 10.2337/dc07-0245

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