Introduction to Commentaries on the Use of Placebo-Controlled Trials of New Therapies in the Treatment of Type 2 Diabetes

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As the editor in chief of *Diabetes Care*, I was stimulated by the thoughtful letter of David S.H. Bell (1) questioning the value and ethics of placebo-controlled trials in the development of new therapeutic agents for the treatment of hyperglycemia in type 2 diabetes, and I decided to look into this issue more in depth. I asked three people to give their perspectives on this issue. The first response, by David Orentlicher (2), is the perspective of a bioethicist who is both a physician and a legal scholar. The second response is from Robert I. Misbin (3), who has spent many years on the front line at the Food and Drug Administration wrestling with this issue. The final response is from Alain D. Baron (4), who has been an outstanding academic clinical investigator and who has recently joined a pharmaceutical firm to apply these skills to the development of a new class of agents for the treatment of type 2 diabetes.

We hope that after reading these thoughtful pieces you will come away with an understanding that this is a complex issue that cannot be categorically answered. Rather, it is the nature and importance of the question being asked that determines whether there needs to be a placebo-controlled trial. If the question is merely "Is this new agent better than what we have already?", then the comparator needs to be an agent or agents of known effectiveness, not a placebo. However, particularly with a new class of agents, the question is often whether the agent is better than nothing. This question can only be answered by a placebo-controlled trial.

Because our armamentarium for the treatment of type 2 diabetes is not ideal, we will need to accept the judgment of the Food and Drug Administration and its Advisory Panel members that at least some new agents will continue to require placebo-controlled trials. Nevertheless, once the "better than nothing" question is answered, subsequent trials, particularly those of substantial length, should have an active comparator.

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