RESPONSE TO COMMENT ON ROSENSTOCK ET AL.

Impact of a Weekly Glucagon-Like Peptide 1 Receptor Agonist, Albiglutide, on Glycemic Control and on Reducing Prandial Insulin Use in Type 2 Diabetes Inadequately Controlled on Multiple Insulin Therapy: A Randomized Trial. Diabetes Care 2020;43:2509–2518

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I thank Dr. Marathe and coauthors, who are part of the superb team of Michael Horowitz and Karen Jones, world-renowned top experts in gastric emptying (1), for recognizing the clinical value of our albiglutide switch study (HARMONY 8), which provided proof of concept for the benefits of using a weekly glucagon-like peptide 1 receptor agonist (GLP-1RA) to simplify an intensive multiple-insulin regimen in patients with long-standing type 2 diabetes previously on basal-bolus insulin (2). We clearly demonstrated that 54% of participants randomized to the albiglutide + basal insulin glargine group were able to replace all prandial insulin without reintroducing insulin lispro, and, for those who still needed prandial insulin, their insulin doses were substantially reduced. Most importantly, improvements of HbA_{1c} to <7% were similar to the levels achieved by the control group, which was randomized to continue with an optimized basal-bolus insulin regimen. However, those on the weekly GLP-1RA regimen improved their glycemic control without increasing hypoglycemia risk and with the added benefit of weight loss compared with the basal-bolus arm (3).

Horowitz, Jones, and colleagues (1) commented on our data and, by focusing on their scholarly expertise on gastric emptying and its impact on postprandial hyperglycemia, honored the proverb "If all you have is a hammer, everything looks like a nail." They correctly assumed that postprandial hyperglycemia was probably the main contributing factor to the baseline HbA_{1c} of 7.8% after optimizing the basal-bolus regimen during the lead-in period before randomization. They postulated that measuring gastric emptying in these patients with type 2 diabetes to determine if the rate of gastric emptying was rapid or slow may help in selecting the type of GLP-1RA to be employed. Contrary to the current belief that long-acting GLP-1RAs have minimal to no sustained effect on gastric emptying due to tachyphylaxis, they mentioned that daily and weekly GLP-1RA may still have some impact on gastric emptying to reduce postprandial hyperglycemia (4,5). Their theoretical concept that those patients with rapid gastric emptying and modest hyperglycemia, such as an HbA_{1c} <8%, may benefit more with a short-acting GLP-1RA, shown to have more sustained and stronger effects on slowing gastric emptying, is interesting and deserves to be tested. However, even with albiglutide, which was probably the weakest of all weekly GLP-1RAs, the HbA_{1c} was reduced from 7.8% to 6.7%, and the total number of insulin injections was more than halved, reduced from 29 to 13 injections per week. Thus, it is highly conceivable that similar or even more robust improvements in HbA_{1c} and greater reductions in the number of prandial insulin injections, hopefully to none, may be achieved with more potent weekly GLP-1RAs such as dulaglutide or semaglutide (6,7). Therefore, measuring gastric emptying is an excellent idea for clinical research purposes, but I believe it is neither essential nor feasible in clinical practice.

Duality of Interest. J.R. has served on advisory panels for Applied Therapeutics, Boehringer Ingelheim, Eli Lilly, Intarcia, Janssen, Novo Nordisk, Oramed, Sanofi, and Zealand and has received research support from Applied Therapeutics, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Genentech, GlaxoSmithKline, Intarcia, Janssen, Lexicon, Merck, Novo Nordisk, Oramed, Pfizer, and Sanofi. No other potential conflicts of interest relevant to this article were reported.

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