RESPONSE TO COMMENT ON HARLAN

Islet Transplantation for Hypoglycemia Unawareness/Severe Hypoglycemia: Caveat Emptor. Diabetes Care 2016;39:1072–1074

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Hering et al. (1) frame their comments around solitary islet transplant's benefit for some of the Clinical Islet Transplantation Consortium phase 3 trial (CIT-07) study's 48 patients with long-standing type 1 diabetes (T1D) and severe hypoglycemic episodes (SHE) (2). I endorsed their assertion that some patients benefited (3).

I framed my commentary (3) in a different light, however. Quoting from the study report (2), CIT-07 was performed "to serve as a license-enabling study" for the U.S. Food and Drug Administration (FDA) as it weighs licensing isolated pancreatic islets as an appropriate therapy for some individuals with T1D. Such licensing decisions are adjudicated by the FDA's Center for Biologics Evaluation and Research, Office of Cellular, Tissue and Gene Therapies. Quoting from the website (4), that committee "reviews and evaluates available data relating to the safety, effectiveness, and appropriate use of. . .human tissues. . .intended for transplantation. . .in the prevention and treatment of a broad spectrum of human diseases [so as to make] appropriate recommendations to the Commissioner of Food and Drugs." The FDA must weigh potential new therapies against the safety and efficacy of currently approved therapies. For instance, since imatinib's remarkable efficacy was demonstrated, any therapy seeking approval for chronic myelogenous leukemia has a higher bar to clear. The FDA decision is particularly difficult for a therapy like islet transplantation with known risks, time-limited benefit for most patients (1–6 years), and great expense.

Approved therapies for T1D continue to advance, and patient outcomes have improved (5,6). The study's contention that islet transplantation helped patients who had "failed expert medical therapy" (1) is hard to support when, of the 48 enrollees, only 21 had ever used a continuous glucose monitor, only 37 had ever used an insulin pump, and two of the enrollees were deemed "medically nonadherent" and should not have been enrolled. The "caveat emptor" of my commentary (3) is built on those facts and that the therapy fairly predictably decreases kidney function and places the individuals at risk for other expected complications associated with immunosuppression and transplantation of allogeneic tissue. Hering et al. (1) also contend that I wrote that islet transplantation would benefit only those "already taking immunosuppressive agents because of having received a kidney transplant." I did not make that claim. Rather, I suggested a specially selected subset of that group as one for whom the risk-benefit calculation might make sense. They write that they "feel" that islet transplantation will result in "a net benefit for some carefully selected patients." While I agree, identifying such patients a priori remains a great challenge, as demonstrated by the CIT-07 study in which at least 2 of the 48 (4%) should never have been enrolled because of nonadherence; perhaps several others would not have continued suffering SHE had modern and much less expensive control tools (e.g., continuous glucose monitors, pumps) been implemented. Hering et al. (1) state that "all available technologies/treatments for T1D. . .should be used before consideration of islet transplantation." I agree, but I worry that licensing isolated islets for transplant may open Pandora's box, i.e., endorsing what appears to be a quick fix for the well-acknowledged difficulties associated with medical therapy for T1D and yet not appropriately accounting for the counterbalancing difficulties associated with isolated islet transplantation.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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