COMMENT ON ERONDU ET AL.

Diabetic Ketoacidosis and Related Events in the Canagliflozin Type 2 Diabetes Clinical Program. Diabetes Care 2015;38:1680–1686

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I read with interest the article by Erondu et al. (1) on the Janssen Research & Development, LLC, experience of diabetic ketoacidosis (DKA) in a canagliflozin series of studies. They reported the characteristics of 12 cases of DKA in their cohort of 17,596 patients in their studies. However, there remain some potentially troubling issues. In their report, they described 4 out of the 12 patients as having DKA, but they did not report the patients' pH, bicarbonate, anion gap, or ketone measurements (and in one of the patients, there was no glucose measurement either). In one patient, they reported glucose and bicarbonate measurements only, and in another, glucose and one "+" of urine ketone only. The question that arises is, how was DKA diagnosed?

The American Diabetes Association (ADA) and U.K. guidelines from the Joint British Diabetes Societies (JBDS) lay out criteria for the definition of DKA, both suggesting that some of these need to be present before a diagnosis of DKA can be made (2,3). If one assumes that the events reported by Erondu et al. were adjudicated and reported as DKA by their safety committee, then it is likely that further biochemistry or clinical data were available but were not shown. However, with the data presented, one would be very hard-pressed to say the patients had DKA. This may mean that the rate of true DKA (as defined by the ADA or JBDS) was actually lower than reported. However, if one assumes that these cases were reported by those local investigators who felt that admissions needed to be reported "come what may," there are also likely to have been a number of other participating centers that had similar cases but because the patients did not have their arterial blood gas measurements recorded or the investigators felt that the patients did not reach the biochemical criteria for DKA, the investigators did not report them as such. This would have led to an underreporting of cases. I would propose that more people would be reluctant to diagnose DKA without biochemically confirming it first. Thus, the true incidence of DKA may be higher than that reported.

This is a situation where full access to the primary data would be necessary. This would enable full transparency and allow clinical judgments and diagnoses to be made based on patient data, not just on those that are released by the company.

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