COMMENT ON WANG ET AL.

# Incretin-Based Therapies and Diabetic Retinopathy: Real-World Evidence in Older U.S. Adults. Diabetes Care 2018;41:1998–2009

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I read with great interest the article by Wang et al. (1) demonstrating that incretin-based therapies used for 1 year do not increase the risk of diabetic retinopathy (DR) compared with other glucose-lowering drugs in a population aged 65 years and older. Beyond these reassuring data, I would like to highlight one striking point. This study offers a quantitative overview of the risk of early worsening of diabetic retinopathy (EWDR) following intensification of treatment (IT) across comparative hypoglycemic groups in real life.

First, physicians must be aware that EWDR is not just a consequence of insulin IT, as initially described in young patients with type 1 diabetes (2). Any therapy leading to a large and rapid drop in glucose may be associated with EWDR in patients with either type 1 or type 2 diabetes (3). Similar recommendations should be applied in all cases.

Second, major risk factors for EWDR include high baseline $HbA_{1c}$ and its magnitude of decrease, in addition to prior DR before IT (4). Even if $HbA_{1c}$ was only available for 10% of this study population, the findings for this subgroup ought to be emphasized. The more patients who had a baseline $HbA_{1c}$ value >9% (75 mmol/mol), the higher the EWDR risk was in the group. While patients initiating a glucagon-like peptide 1 receptor agonist versus long-acting insulin or versus thiazolinediones had EWDR rates of 7 and 12.3 per 1,000 person-years, respectively (see Table 2 in Wang et al. [1]), fewer patients in the first cohort (19.6%) had an $HbA_{1c}$ value >9% (75 mmol/mol) compared with the second cohort (26.3%) (see Table 1 [1]). Thus, EWDR risk seems more related to the $HbA_{1c}$ level before IT than to the therapeutic class itself. Moreover, the DR event rate was highest early after IT and decreased thereafter (from 10–20 per 1,000 person-years for a duration of use <6 months to 4–9 per 1,000 person-years for a duration of use >12 months) (see Table 3 [1]), suggesting a transient phenomenon, as observed in previous studies (2,5), that is counterbalanced by long-term DR reduction with improved glucose control.

Finally, Wang et al. (1) found about a threefold increase in EWDR risk in patients with $HbA_{1c}$ >9% (75 mmol/mol) compared with those with $HbA_{1c}$ <7% (53 mmol/mol) (see Supplementary Table 6 [1]) and a sixfold increase in patients with baseline DR versus no preexisting DR (see Table 3 [1]). Given the consequences of such results in everyday clinical practice, careful retinal examination should be performed in patients before IT, particularly in those with uncontrolled diabetes and preexisting DR, whatever the glucose-lowering treatment. Close eye monitoring may also be recommended during the first year following IT in patients at high risk.

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

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