Effects of Dulaglutide and Insulin Glargine on Estimated Glomerular Filtration Rate in a Real-World Setting

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ABSTRACT

Purpose: The aims of this study were to use real-world treatment results to compare changes in estimated glomerular filtration rate (eGFR) and glycosylated hemoglobin (HbA_{1c}) among patients with type 2 diabetes who initiated treatment with dulaglutide or insulin glargine and to determine the proportions of patients with renal impairment who initiate each treatment.

Methods: The study used data from the Practice Fusion electronic health records database from October 2013 through June 2017. Adults with type 2 diabetes who initiated dulaglutide or insulin glargine therapy and had multiple recorded serum creatinine and/or HbA_{1c} laboratory test results were included in the study. The dulaglutide cohort (n = 1222) was matched to the insulin glargine cohort (n = 13,869) using Mahalanobis distance matching with propensity score calipers. Multivariable analyses of the matched cohorts of individuals with serum creatinine results (n = 1183 dulaglutide and 1183 insulin glargine) examined the association between intent-to-treat therapy and changes in eGFR. In addition, multivariable analyses were also conducted on a subset of these patients who also had recorded HbA_{1c} tests (n = 1088 dulaglutide and 1088 insulin glargine) to examine the association between changes in HbA_{1c} during the 1 year postperiod.

Findings: Among patients who initiated dulaglutide therapy, only 0.9% of patients had an index eGFR <30 and ≥15 mL/min/1.73 m^2 and 0.1% had an index eGFR <15 mL/min/1.73 m^2. In contrast, 4.1% of insulin glargine–treated patients had an index eGFR <30 and ≥15 mL/min/1.73 m^2 and 1.2% had an index eGFR <15 mL/min/1.73 m^2. Compared with patients who initiated therapy with insulin glargine, initiation of dulaglutide therapy was associated with a significantly smaller decrease in eGFR (−0.4 vs −0.9 mL/min/1.73 m^2; $P = 0.0024$), a significantly smaller likelihood of having a 30% or greater reduction in eGFR (3.3% vs 4.1%; $P < 0.0001$), and a significantly larger reduction in HbA_{1c} (−0.5% vs −0.2%; $P < 0.0001$).

Implications: In clinical practice, the use of dulaglutide was relatively more limited in patients with a higher degree of renal impairment compared with use of insulin glargine. However, initiation of dulaglutide therapy, compared with insulin glargine therapy, was associated with a significantly smaller decrease in eGFR and a larger reduction in HbA_{1c} during the 1 year postperiod. (*Clin Ther.* 2018;■:1–12)

Key words: dulaglutide, estimated glomerular filtration rate, glycosylated hemoglobin, insulin glargine.

INTRODUCTION

The American Diabetes Association suggests that glucagon-like peptide-1 receptor agonist (GLP-1 RA) drugs may be used as first-line therapy for type 2 diabetes (T2D) if metformin is contraindicated or not well tolerated. The GLP-1 RA class of medications should also be considered for use in combination with

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metformin and/or basal insulin if the patient's glycosylated hemoglobin (HbA_{1c}) concentration is ≥9% initially or if it is not controlled after 3 months of therapy.[1] This newer class of injectable, antidiabetic drugs lowers HbA_{1c} with a low risk of hypoglycemia while promoting weight loss.[2] However, the effect of GLP-1 RA therapy on kidney function is less well known. Kidney function is of considerable concern for patients with T2D, given that 20% of these patients have kidney damage (nephropathy) caused by chronic hyperglycemia and 20% of those with T2D and nephropathy will eventually develop chronic kidney disease (CKD).[3]

Animal studies have found that GLP-1 RA therapies have a protective effect on the kidneys,[4,5] whereas clinical studies have found GLP-1 RA therapy to be associated with no decline in kidney function[6,7] or with slower decline relative to a placebo and/or other comparators, especially in patients with reduced kidney function.[8,9] The recent Assessment of Weekly Administration of LY2189265 (dulaglutide) in Diabetes 7 (AWARD-7) trial compared once-weekly dulaglutide with titrated daily insulin glargine, both in conjunction with insulin lispro, in people with T2D and comorbid CKD.[8] In AWARD-7, dulaglutide had the same glucose-lowering effect as insulin glargine, whereas patients taking dulaglutide had greater weight loss, fewer episodes of hypoglycemia, and a slower decrease in estimated glomerular filtration rate (eGFR).[8,10] However, the prescribing information for GLP-1 RAs includes warnings of reports of "acute renal failure and worsening of chronic renal failure," especially in patients experiencing nausea, vomiting, diarrhea, or dehydration.[11,12] Prescribing information for GLP-1 RAs also urges practitioners to use caution when initiating or escalating doses in patients with renal impairment and to monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions.[11,12]

The goals of the present study were to use real-world treatment results to compare changes in kidney function and glycemic control among patients with T2D who initiated treatment with dulaglutide or insulin glargine and to determine proportions of patients with renal impairment who initiate each treatment. To this end, we used retrospective data from electronic health records (EHRs) to compare the outcomes of patients who were prescribed insulin glargine or dulaglutide to treat their T2D. In comparing these patient groups, the study examined changes in eGFR and HbA_{1c} for patients treated with dulaglutide or insulin glargine.

METHODS

The data for this project came from the Practice Fusion EHR database and covered the period from October 2013 through June 2017. Practice Fusion has the largest real-time health care database in the United States, with records from >112,000 medical professionals and >5 million patient visits per month. The data come primarily from smaller practices (≤10 physicians) with a 40/60 split between primary care physicians and specialists. The database contains information on patient characteristics, diagnoses, prescriptions, encounter type, prescription orders, laboratory test results, and vital signs. The data are compliant with the Health Insurance Portability and Accountability Act. Given that the data were fully deidentified, no internal review board approval or patient authorization was required.

To be included in the study, patients were first identified as having T2D, based on a previously validated algorithm for use with EHR.[13] To begin with, the patient needed to have at least one diagnosis of diabetes (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] code of 250.xx or *International Classification of Diseases, Tenth Revision, Clinical Modification* [ICD-10-CM] code of E10xx or E11xx). Patients with diabetes were excluded if they were identified with type 1 diabetes (T1D) based on the following criteria: (1) a ratio of the number of T1D to T2D diagnoses >0.5 and a prescription for glucagon, (2) a ratio of the number of T1D to T2D diagnoses >0.5 and no prescription for any oral glucose-lowering agent (GLA) other than metformin, (3) a diagnosis as C-peptide negative, (4) a positive diagnosis for diabetes autoantibodies, or (5) a prescription for urine acetone test strips. The remaining patients were classified as having T2D.

Patients who met the above requirements also needed to have been prescribed dulaglutide or insulin glargine from October 25, 2013, through June 18, 2016, with the date of the first such use identified as the index date. Patients were also required to have received at least one serum creatinine (S_{cr}) laboratory test in 13 months before the index date (eg, the preperiod) and another in the 12 months after the index date