Glycemic Control and Weight Outcomes for Exenatide Once Weekly Versus Liraglutide in Patients with Type 2 Diabetes: A 1-Year Retrospective Cohort Analysis

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ABSTRACT

Purpose: Data comparing real-world effectiveness of the glucagon-like peptide-1 receptor agonists (GLP-1RAs) exenatide once weekly (QW) and liraglutide in the treatment of type 2 diabetes (T2D) are limited. Furthermore, there is limited information on exenatide QW or liraglutide response by glycemic control and insulin use status. This study identifies 1-year glycosylated hemoglobin (HbA_{1c}) and weight outcomes with exenatide QW and liraglutide in the real-world setting overall and in insulin-naive patients with uncontrolled T2D.

Methods: This retrospective cohort study using national electronic medical record data compared 1-year HbA_{1c} and weight outcomes in patients with T2D prescribed exenatide QW or liraglutide. Included patients were adults (≥18 years old) with T2D who were GLP-1RA naive when newly prescribed exenatide QW or liraglutide between January 1, 2012, and March 31, 2013 (index date). Outcomes were reported descriptively overall and in subsets of insulin-naive patients with baseline HbA_{1c} ≥7.0% or ≥9.0%. Multivariable linear regression analyses were performed to estimate adjusted change in HbA_{1c} and weight.

Findings: The study included 808 exenatide QW and 4333 liraglutide patients. Mean (SD) age was 57 (11) years in both groups. Mean baseline HbA_{1c} was 8.3% (1.5%) in exenatide QW patients and 8.4% (1.6%) in liraglutide patients ($P = 0.66$); 16 (2%) of the exenatide QW and 1099 (25.4%) of the liraglutide patients were newly prescribed insulin on the index date ($P < 0.001$). Adjusted mean HbA_{1c} change at 1 year was −0.37% (95% CI, −0.53% to −0.21%) for exenatide QW and −0.37% (95% CI, −0.55% to −0.18%) for liraglutide. Adjusted HbA_{1c} reduction was more pronounced in insulin-naive patients with baseline HbA_{1c} ≥7.0% (−0.71% and −0.80% for the exenatide QW and liraglutide patients, respectively, $P > 0.05$) and ≥9.0% (−1.73% and −1.57% for exenatide QW and liraglutide patients, respectively, $P > 0.05$). Mean (adjusted) weight loss was −2.22 kg (95% CI, −3.06 to −1.37 kg) with exenatide QW and −2.21 kg (95% CI, −3.18 to −1.23 kg) with liraglutide.

Implications: Exenatide QW and liraglutide lead to similar HbA_{1c} and weight reductions at 1 year in the real-world setting. Greater HbA_{1c} reductions occurred in insulin-naive patients with baseline HbA_{1c} ≥7.0%. Both agents are appropriate options for patients needing antidiabetes therapy to lower HbA_{1c} while promoting weight loss. (*Clin Ther*. 2016;38:2642–2651) © 2016 The Authors. Published by Elsevier HS Journals, Inc.

Key words: diabetes mellitus, exenatide, glycemic control, liraglutide, observational study, weight.

INTRODUCTION

Effective management of type 2 diabetes (T2D) can be a significant challenge for patients, practitioners, and

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health care systems. T2D is a progressive disease associated with high comorbidity.[1] Thus, even adherent patients eventually require multiple diabetes medications to manage hyperglycemia and reduce the risk of developing diabetes complications. Although consistent in recommending metformin as first-line therapy, guidelines are less specific with second-line treatment, recommending that practitioners select second-line therapy based on patient-specific treatment goals and product characteristics.[2,3]

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are beneficial as second-line T2D therapeutic alternatives because they are associated with significant reductions in glycosylated hemoglobin (HbA_{1c}) and weight with low risk of hypoglycemia.[2] Numerous GLP-1RAs are approved for treatment of T2D. Exenatide dosed BID was the first GLP-1RA, approved in 2005. Exenatide BID targets mealtime, or postprandial, glucose and is approved as add-on treatment to basal insulin based on complementary pharmacologic effects on prandial and fasting glycemia.[4] Liraglutide dosed once daily was the second GLP-1RA approved (2010), followed by a once-weekly (QW) formulation of exenatide (2012). Albiglutide and dulaglutide were approved in late 2014; both are dosed once weekly.

Exenatide QW[5] and liraglutide[6] are GLP-1RAs commonly used in the United States. They are indicated as add-on therapy adjunct to diet and exercise to improve glycemic control in adults with T2D. Clinical trials have found both agents to be effective and generally well tolerated.[7,8] Although they differ in injection frequency, differentiation in terms of efficacy and tolerability is complex but limited because of mixed evidence.[7,9] A head-to-head comparison of liraglutide versus exenatide QW found a small but statistically greater HbA_{1c} reduction of 0.21% (95% CI, 0.08–0.33) for liraglutide versus exenatide QW.[9] Common adverse events were reported more often in the liraglutide group, including nausea, diarrhea, and vomiting. Furthermore, more patients taking liraglutide than exenatide QW discontinued the study because of adverse events.[9] A recent medication adherence study found that patients receiving exenatide QW were more likely to be adherent than patients receiving liraglutide.[10]

Given the differences in tolerability and adherence, we hypothesized the differences in HbA_{1c} outcomes between exenatide QW and liraglutide seen in the head-to-head clinical trial may not be observed in a real-world setting. A prior study evaluated glycemic control and weight outcomes of exenatide QW versus liraglutide,[11] but the study outcome period was limited to 6 months. Furthermore, there is limited information on response to exenatide QW or liraglutide according to glycemic control and insulin use status, which would be of use to prescribers considering the addition of GLP-1RA to therapy. Therefore, the purpose of this study was to compare real-world HbA_{1c} and weight outcomes at 1 year in patients with T2D prescribed exenatide QW or liraglutide overall and in subsets of insulin-naive patients with uncontrolled T2D.

PATIENTS AND METHODS

Study Design and Timeline

A retrospective cohort study was conducted using a national electronic medical record database to assess 1-year HbA_{1c} and weight outcomes in adult patients with T2D newly prescribed exenatide QW or liraglutide between January 1, 2012, and March 31, 2013.

Data Source

This study used the Quintiles electronic medical record (Q-EMR) database, a national ambulatory care dataset. At the time of this study, Q-EMR included patient-level data on >38 million individuals from 49 states and the District of Columbia. Q-EMR includes demographic data, vital signs, *International Classification of Diseases, Ninth Revision* (ICD-9) –based medical diagnoses, laboratory tests and results, procedures, insurance information, prescription medication orders, and medication history. Data were available through March 31, 2014.

Cohort Selection

The study cohort was drawn from adult patients with a diagnosis of T2D (ICD-9 codes 250.*0 or 250.*2, taking a diabetes drug, $HbA_{1c} \geq 6.5\%$, or 2 consecutive fasting blood glucose values ≥126 mg/dL). Included patients were GLP-1RA naive when newly prescribed exenatide QW or liraglutide between January 1, 2012, and March 31, 2013 (index date), which allowed for identification of baseline characteristics before the index date and 1-year outcomes data using the available data. Included patients had HbA_{1c} values on the index date (−60 to +30 days) and