Real World Use of Exenatide Once-Weekly Compared to Basal Insulin among Type 2 Diabetic Patients with Renal Impairment

A.M. Loughlin[1], Q. Qiao[2], K.M. Johnsson[2], S. Grandy[3], S. Ezzy[1], L. Yochum[1], C.R. Clifford[1], R. Gately[1], A.P. Nunes[1], D.D. Dore[1], and J.D. Seeger[1]

Optum Epidemiology, Waltham, MA. USA[1], AstraZeneca, Gothenburg Sweden[2], AstraZeneca, Gaithersburg, MD USA[3]

1053-P

Introduction

- Exenatide once-weekly (EQW) is a glucagon-like peptide-1 receptor agonist treatment for patients with type-2 diabetes (T2D).
- EQW is an alternative to basal insulin (BI) when considering a first injectable therapy.
- EQW is administered in a 2 mg dose, with no dose titration.
- EQW is excreted through the kidney, no dose alteration has been recommended, and EQW is not recommended for patients with severe renal impairment.
- Little is known about the benefit and risk of using EQW compared with BI in T2D patients with renal impairment.

Objective

To evaluate the effectiveness and tolerability of EQW and BI in T2D patients by level of renal function.

Data Source

Humedica Research Database: An electronic health record (EHR) database that includes patient-level data from healthcare encounters (including diagnoses, procedures, medications, clinical measures, and clinical notes). The database represents a geographically diverse US population, over 25,000 physicians, and over 25 million patients.

Methods

- Retrospective cohort study including T2D patients (ICD-9: 250.x0 or 250.x2) enrolled in the EHR database between January 2012 and January 2015 with follow-up through March 2015.
- Eligible patients were injectable-naïve initiators of EQW or BI, with 6-months observed EHR data prior to initiation.
- EQW initiators were matched in a variable ratio (up to 1:2) to BI initiators by estimated propensity score using logistic regression and greedy matching.
- Clinical measurements and laboratory values were extracted from EHR, and summarized at baseline and within standard intervals over the first year following initiation of study drug.
- Hemoglobin A1c (HbA1c), body weight (WT), serum creatinine, estimated glomerular filtration rate (eGFR), urine albumin/creatinine ratio (ACR) were identified at baseline and quarterly (Q1 to Q4) in the first year.

Methods (continued)

- Summary clinical or laboratory measures were taken as the mean of values within an interval. If no values were observed, values were multiply-imputed (5-imputations) using fully conditional specification method.
- Gastrointestinal (GI) symptoms (nausea and vomiting, diarrhea and constipation) were identified by diagnostic codes.
- Hypoglycemia was identified by diagnostic codes and natural language processing of clinical notes.

Analysis Plan

- **Measurement of Effectiveness: HbA1c and WT –** assessed by the mean change from baseline, or mean percent change from baseline and the 95% confidence intervals (CI) for each.
- **Measure of Occurrence: GI symptoms and hypoglycemia –** assessed by the frequency of first event in follow-up, and the incidence rate (95% CI) per person-year censored at first event. Cohorts were compared using relative rates (RR) (95% CI).
- **Renal Impairment Stratification—eGFR***
  - Normal: eGFR ≥ 90.00 mL/min/1.73m^2
  - Mild: 60.00 ≤ eGFR ≤ 89.99 mL/min/1.73m^2
  - Moderate-Severe: eGFR ≤ 59.99 mL/min/1.73m^2

*eGFR was calculated using serum creatinine, sex, and race using the CKD-EPI Equation (*Ann Intern Med 2009; 150:604-612*)

Results

- We compared propensity score matched cohorts of EQW (n=1,005) and BI (n=1,944) initiators.
- Average length of follow-up was 1.7 person-years for both EQW and BI cohorts.
- Baseline characteristics in the matched cohorts were similar (Table 1). The cohorts were balanced on demographics, health utilization, health history, diagnostic and procedure codes, and medication found to be associated within receipt of EQW compared to BI, in propensity score matched analysis.

Table 1. Comparison of Baseline Characteristics

	EQW	BI
Baseline Characteristic	**N (%)**	**N (%)**
Body Mass Index (kg/m^2)		
Underweight/Normal weight (<24)	13 (1.3)	36 (1.9)
Overweight (25-29)	130 (12.9)	290 (14.9)
Obese (30-39)	522 (51.9)	1,028 (52.9)
Morbidly obese (≥40)	340 (33.8)	590 (30.3)
Renal Impairment -- eGFR		
Normal	480 (47.8)	913 (47.0)
Mild	379 (38.0)	727 (37.4)
Moderate-Severe	112 (11.0)	245 (12.6)
Not Available†	34 (3.0)	59 (3.0)
Hemoglobin A1c		
≤ 7.0%	260 (25.9)	485 (24.9)
7.1-9.0%	463 (46.1)	880 (45.3)
> 9.0%	282 (28.1)	579 (29.8)

† When race was unknown estimated glomerular filtration rate (eGFR) was not calculated

Effectiveness

Figure 1. Mean Percent Change from Baseline for Hemoglobin A1c %, by Renal Function, and by Quarter (Q1-Q4).

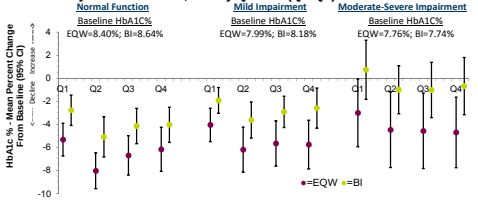
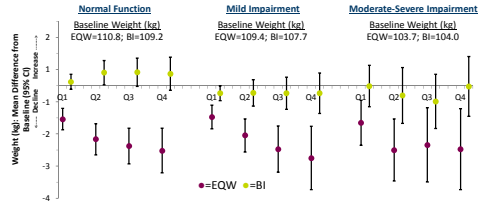


Figure 2. Mean Difference from Baseline for Body Weight, By Renal Function and Quarter (Q1-Q4).



Tolerability

Figure 3. eGFR Stability by Renal Function and Quarter (Q1-Q4).

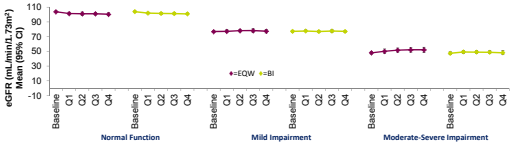


Figure 4. Urine ACR Stability by Renal Function and Quarter (Q1-Q4).

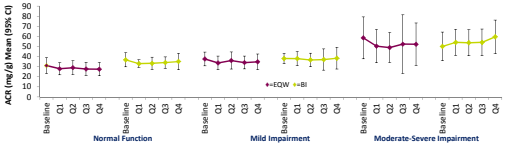
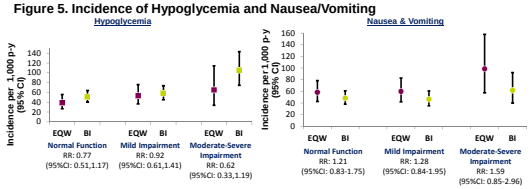


Figure 5. Incidence of Hypoglycemia and Nausea/Vomiting



Conclusions

- Declines in HbA1c were numerically greater in EQW relative to BI. The decline was greatest in patients with normal renal function.
- Weight was reduced with EQW compared to BI, regardless of renal function. The difference was greatest among persons with normal or mildly impaired renal function.
- Renal function remained stable in both EQW and BI initiators in the year following initiation.
- Hypoglycemia occurred less often among EQW compared to BI, and nausea and vomiting occurred more often, yet confidence intervals overlapped. The incidence of each increased with level of renal impairment, regardless of treatment.

Supported by AstraZeneca