Clinical Study Report Synopsis

Drug Substance	Exenatide
Study Code	D5551R00012
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Comparative Effectiveness of Exenatide QW vs. Insulin Glargine on Economic Outcomes in Patients with Type 2 Diabetes Who Initiate Injectable Therapy

Study dates: First subject enrolled: 1 Jul 2015
Last subject last visit: 30 Jun 2016

Phase of development: Therapeutic use (IV)

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

Study centre(s)

One study centre and one country (US)

Publications

Wittbrodt E, Kong AM, Moore-Schiltz L, Juneau P. All-cause and diabetes-related healthcare costs among U.S. adults with type 2 diabetes initiating exenatide once weekly or insulin glargine. *Diabetes Obes Metab* 2017 Oct 30; doi: 10.1111/dom.13145. [Epub ahead of print]. (manuscript)

Kong AM, **Wittbrodt E**, Moore-Schiltz L, Juneau P. Health-care utilization and costs in patients initiating exenatide once weekly compared with insulin glargine. *Diabetes* 2017; 66(Supplement 1):A362. (abstract)

Objectives and criteria for evaluation

Table S1 Objectives and outcome variables

Objective			Outcome Variable
Priority	**Type**	**Description**	**Description**
Primary	HEOR	Diabetes-related healthcare resource utilization and costs of EQW* vs IG**	DM-related HCRU and costs
Secondary	HEOR	Overall healthcare resource utilization and costs of EQW vs IG	Overall HCRU and costs
		Major adverse cardiovascular event (MACE)-related healthcare utilization and costs of EQW vs IG	MACE-related HCRU and costs
		Rates and costs of medically attended hypoglycemia of EQW vs IG	Hypoglycemia rates and costs

*EQW = exenatide once weekly

**IG = insulin glargine

Study design

- Retrospective database analysis of the MarketScan® Commercial Claims and Encounters Database
    - Consists of employer- and health plan-sourced data containing medical and drug data for several million individuals annually
    - For data year 2014, the Commercial Database contains 36.5 million covered lives, encompassing employees, their spouses, and dependents
    - Medical claims are linked to outpatient prescription drug claims and person-level enrollment information.
- MarketScan® Medicare Supplemental Database
    - The first in the United States to profile the healthcare experience of retirees with Medicare supplemental insurance paid for by employers.
    - Includes the Medicare covered portion of payment (represented as Coordination of Benefits Amount, or COB), the employer-paid portion, and any out-of-pocket patient expenses.
    - For data year 2014, the Medicare Database contains 3.6 million covered lives
- MarketScan® Lab Database
    - Adds laboratory results to the data elements contained in the Commercial and Medicare Supplemental Databases.
    - The tests for which results are available include hematocrit, glucose random, hemoglobin A1C, potassium serum, creatinine serum, sodium serum, BUN, cholesterol total serum, triglyceride, HDL cholesterol, LDL cholesterol, and calcium serum.
- Quintiles EMR Database
    - Large, centralized, national network of outpatient offices whose providers make their de-identified patient-level data available for research

- Available data include demographics, vital signs, ICD-9-CM-based medical diagnoses, patient complaints, detailed physician notes, diagnostic tests and results, procedures, and insurance and prescription information.

- Laboratory test orders and results, lifestyle characteristics, and patient data from specialty healthcare providers are also available

- As of December 2014, the Q-EMR network contained data on more than 39 million patients, from more than 725 member institutions and more than 39,000 providers.

Target subject population and sample size

- Patients meeting the following study eligibility requirements were selected into the study:

  - At least one or more outpatient prescription claim for EQW or IG between February 1, 2012 – June 30, 2014 (first prescription is the index date)

  - At least 18 years of age as of the index date

  - Continuous enrollment with medical and pharmacy benefits for at least 12 months before the index date and at least 12 months after the index date

  - Patient with one or more medical claim with a diagnosis code for T2DM (ICD-9-CM 250.x0 or 250.x2 in the baseline period or on the index date

  - Patients without outpatient prescription claims for any injectable glucose-lowering medication during the baseline period (GLP-1RA or insulins)

  - Patient with no medical diagnosis (or procedure) code indicative for Type 1 diabetes mellitus (ICD-9-CM 250.x1 or 250.x3, gestational diabetes (ICD-9-CM 648.8x), or pregnancy or childbirth in the baseline or follow-up periods.

  - Patients without combination EQW and IG therapy at index

Duration of treatment

Patients were followed for 12 months after the index date (date of first prescription for EQW or IG).

Statistical methods

For the descriptive analyses, baseline patient characteristics were compared between the two cohorts using *t*-tests for continuous variables and chi-squared tests for categorical variables, with p-values <0.05 considered statistically significant. Given the differences in patient

characteristics between the two cohorts at baseline, propensity score matching was utilized to balance the cohorts. A logistic regression model was fit where membership in the EQW cohort was the outcome and the predictors were baseline characteristics. Propensity scores were generated from this model. Patients in the IG cohort were then matched 1:1 to patients in the EQW cohort using the nearest neighbor technique. The balance achieved by the match was assessed using standardized differences. Variables with a standardized difference <10 were considered balanced. In a sensitivity analysis, a 1:3 match between EQW and IG initiators was also conducted. Following the match, logistic regression models were fit to compare odds of inpatient admissions and emergency room visits, and ordinary least-squares regression models with a log transformation were fit to model differences in costs between the matched cohorts. Any patient characteristics that were unbalanced after matching were included as covariates in the models. If all patient characteristics were balanced, no covariates were included.

Subject population

There were over 600,000 patients in the MarketScan databases who had ≥1 claim for either EQW or IG from February 1, 2012, through June 30, 2014. After applying the inclusion and exclusion criteria, there were 7,749 EQW initiators and 40,178 IG initiators. When comparing the unmatched patient cohorts, there were significant differences in baseline characteristics between EQW initiators and IG initiators. The EQW cohort was younger and had a larger proportion of women. Additionally, the EQW cohort tended to be healthier than IG initiators, with lower average DCI and aDCSI scores and lower proportions of patients with macrovascular or microvascular complications and renal impairment. Use of metformin in the baseline period was more frequent among EQW initiators, although it was prevalent among both cohorts. In addition, the use of sulfonylureas was more frequent among IG initiators.

While baseline total healthcare costs were lower on average for the EQW cohort, average costs and copayments for antidiabetes medications, including the copayment on the index claim, were lower for the IG cohorts.

Summary of efficacy results

In unmatched analyses, the proportions of patients with an all-cause or diabetes-related inpatient admission over the 12-month follow-up period were lower in the EQW cohort compared with the IG cohort. This was also true for all-cause and diabetes-related emergency room visits. Mean all-cause costs in the 12-month follow-up period were numerically higher for IG initiators compared with EQW initiators, while the medians differed by approximately $500. All-cause pharmacy costs accounted for 46% of total costs in the EQW cohort compared with 26% of costs in the IG cohort. Among the IG cohort, all-cause inpatient costs accounted for 27% of total costs, while inpatient costs for the EQW cohort accounted for 14% of total costs. Mean total diabetes-related costs were also lower for EQW initiators; however, median costs were numerically higher for EQW initiators. For the EQW cohort, antidiabetes medication costs and diabetes-related inpatient costs accounted for 57% and 22% of total diabetes-related costs, respectively. For the IG cohort, antidiabetes medication costs and diabetes-related inpatient costs accounted for 30% and 44% of total diabetes-related costs, respectively.

After matching 1:1, there were 7,749 patients in each cohort. All patient characteristics included in the propensity score were balanced, with standardized differences <10; therefore, subsequent models were fit without the covariates employed in the original logistic regression model used to estimate propensity scores. In logistic regression models fit on the matched

sample, EQW initiators had significantly lower odds of experiencing an all-cause inpatient admission by 26%, diabetes-related inpatient admission by 28%, and diabetes-related inpatient admission or emergency room visits during follow-up by 22%. In cost models fit on the matched sample, all-cause and diabetes-related medical costs were significantly lower for EQW initiators than IG initiators by approximately $100 and $800, respectively. However, all-cause total costs and diabetes-related total costs were significantly higher for EQW initiators, driven by a significant difference in pharmacy costs. Both all-cause and diabetes-related pharmacy costs were significantly higher for EQW patients compared to IG patients with differences of approximately $2,800 for all-cause pharmacy costs and $1,900 for diabetes-related pharmacy costs. Results using a 1:3 match were similar. The models fit on the 1:3 matched sample included copayment on index claim as a covariate because it was unbalanced after matching.

Conclusion(s)

In conclusion, adults with T2D who initiated EQW had lower odds of all-cause and diabetes-related inpatient admission and lower all-cause and diabetes-related medical costs than patients who initiated IG. Overall, EQW initiators had higher all-cause and diabetes-related total costs than IG initiators, due to higher pharmacy cost.