Clinical Study Report Synopsis	
Drug Substance	Dapagliflozin
Study Code	D1690R00034
Edition Number	1
Date	30 Apr 2018
EudraCT Number	<<>>
NCT Number	<<>>

Comparison of Healthcare Resource Utilization and Costs in Type 2 Diabetes Patients Initiating Dapagliflozin versus Sitagliptin

Study dates: First subject enrolled: 31 Mar 2017
Last subject last visit: 30 Apr 2017

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 ET, Parker ED, McPheeters J. Health Care Utilization and Costs in Patients with T2D Treated with Dapagliflozin or Sitagliptin in a US Managed Care Setting. *WCIRDC 2017: 15th World Congress on the Insulin Resistance Diabetes & Cardiovascular Disease – November 30–December 2, 2017; Los Angeles, California, USA* [Poster presentation]

Objectives and criteria for evaluation

Table S1 Objectives and outcome variables

Objective			Outcome Variable
Priority	**Type**	**Description**	**Description**
Primary	HEOR	All-cause healthcare resource utilization and costs of dapagliflozin vs sitagliptin	All-cause HCRU and costs
Secondary	HEOR	Diabetes-related resource utilization and costs of dapagliflozin vs sitagliptin	DM-related HCRU and costs

Study design

- Retrospective database analysis of the Optum Research Database [ORD] or IMPACT database) or Medicare Advantage with Part D coverage.
    - The ORD and IMPACT databases combined have approximately 51.8 million enrollees and are geographically diverse and representative of the US commercially insured population.
    - Contains medical and outpatient pharmacy claims

Target subject population and sample size

- Patients meeting the following study eligibility requirements were selected into the study:
    - ≥1 prescription claim for either dapagliflozin or sitagliptin between January 01, 2014 and April 30, 2015 (identification period).
    - At least 18 years of age as of the index date

- Continuous enrollment with medical and pharmacy benefits for at least 6 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 SGLT-2 inhibitor or DPP-4 inhibitor
- 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.

Duration of treatment

Patients were followed for 12 months after the index date (date of first prescription claim for dapagliflozin or sitagliptin).

Statistical methods

Study variables were analyzed descriptively for dapagliflozin and sitagliptin patients. Numbers and percentages were provided for categorical variables and means and standard deviations were provided for continuous variables. The standardized mean difference (SMD) was calculated for propensity score matching variables and outcome variables were compared using tests for paired data (paired *t*-tests, signed rank tests, McNemar's test). All analyses were also conducted separately for the subgroup of patients with evidence of OAD monotherapy use in the baseline period.

Due to a remaining imbalance in baseline total healthcare costs between dapagliflozin and sitagliptin initiators after propensity score matching, a generalized linear model (GLM) with a gamma distribution and log link, adjusting for baseline total all-cause healthcare costs was run to compare follow-up costs between the two cohorts. Additionally, sensitivity analyses were conducted to adjust for baseline differences in DCSI across the cohorts.

Subject population

A total of 3,269 dapagliflozin initiators and 8,702 sitagliptin initiators were propensity-score matched, leaving 2,722 patients in each cohort. The cohorts were well matched. Mean age was 53 years among dapagliflozin initiators and 54 years among sitagliptin initiators (SMD=5.80%) and a slight majority of patients were male in both cohorts (57.9% dapagliflozin, 57.0% sitagliptin; SMD=1.93%) (Table 1). The mean Quan-Charlson comorbidity score was approximately 0.5 for both cohorts (SMD=5.10%). The difference in DCSI scores approached significance, with sitagliptin initiators having higher scores than patients who initiated dapagliflozin (SMD=9.96%).

In the matched cohorts during the baseline period, 13% of patients had no evidence of treatment, 23% of patients received insulin, 34% received OAD monotherapy and 31% received injectable therapy either alone (5%) or in combination with an OAD (23%) or another injectable (3%). Of the 1,842 patients on monotherapy during baseline, 85% were on metformin, 14% on SU, and 1% on TZD. Patients in both cohorts used an average of 1.13 (±0.77) OADs during the baseline period.

Baseline all-cause and diabetes-related healthcare resource utilizations were similar among the dapagliflozin and sitagliptin cohorts after propensity score matching, with the exception of all-cause outpatient visits (1.65 versus 2.14, respectively; SMD=11.35), all-cause inpatient stays (mean count=0.4 versus 0.6, respectively; SMD=11.72), and diabetes-related inpatient stays (0.3 versus 0.6, respectively; SMD=11.60).

Differences in baseline healthcare costs also remained despite propensity score matching. Both all-cause medical costs ($5,186 versus $3,534, SMD=11.99) and diabetes-related medical costs ($3,005 versus $1,736, SMD=11.54) were higher in the sitagliptin versus dapagliflozin cohort. Conversely, dapagliflozin users had higher diabetes-related baseline pharmacy costs compared with sitagliptin users ($882 versus $653, SMD=15.45).

Summary of efficacy results

Healthcare Utilization and Costs

During the 1-year follow-up period, sitagliptin initiators had significantly more all-cause office visits (11.3 versus 10.5, p=0.003), all-cause outpatient visits (4.3 versus 3.5, p<0.001), all-cause inpatient stays (0.1 versus 0.09, p=0.029), and diabetes-related office visits (4.6 versus 4.4, p=0.003) compared with dapagliflozin initiators, whereas dapagliflozin patients had more all-cause (49.1 versus 46.4, p<0.001) and diabetes-related (16.9 versus 14.6, p<0.001) pharmacy fills.

In the 1-year follow-up period, total all-cause healthcare costs were similar between the two cohorts. Compared with dapagliflozin initiators, patients who initiated sitagliptin had higher costs for office visits ($2,023 versus $1,684, p=0.01) and outpatient visits ($4,179 versus $3,239, p=0.003). The higher medical costs in sitagliptin patients were balanced by higher pharmacy costs in dapagliflozin initiators ($7,295 versus $6,749, p=0.006), resulting in no difference in all-cause total costs. Diabetes-related healthcare costs followed a similar pattern, with no overall cost difference between the cohorts. Sitagliptin initiators had higher costs for

diabetes-related office visits ($658 versus $592, p=0.034), whereas dapagliflozin initiators had higher diabetes-related pharmacy costs comparatively ($4,830 versus $4,081, p<0.001).

After adjusting for baseline total healthcare costs, patients on dapagliflozin had 13.5% lower all-cause medical costs (cost ratio=0.865, p=0.042) compared with sitagliptin patients, but had 7.8% higher pharmacy costs (cost ratio=1.078, p=0.012), resulting in no significant difference in total follow-up healthcare costs between the cohorts (cost ratio=0.950, p=0.256). In a sensitivity analysis that adjusted for both baseline total all-cause healthcare costs and DCSI score, follow-up healthcare costs remained similar between the cohorts (cost ratio=0.976, p=0.557). Medical costs no longer differed between patients who initiated sitagliptin versus dapagliflozin (cost ratio=0.906, p=0.128); however, pharmacy costs remained higher among dapagliflozin initiators (cost ratio=1.082, p=0.009).

A subgroup analysis included 1,804 patients (902 per cohort) who had OAD monotherapy use at baseline, of whom 85% had pharmacy claims for metformin, 14% had claims for an SU, and 1% were on a TZD during the baseline period. Compared with patients who initiated dapagliflozin, sitagliptin patients had higher total all-cause healthcare costs ($14,884 versus $12,353, p=0.026), including higher office visit costs ($2,078 versus $1,323, p=0.003) over the follow-up period. In contrast, total diabetes-related healthcare costs were similar between the dapagliflozin and sitagliptin cohorts ($6,750 versus $7,383, p=0.399), as the higher diabetes-related office visit costs ($542 versus $458, p<0.001) among sitagliptin patients were offset by the higher diabetes-related pharmacy costs ($3,123 versus $2,837, p=0.015) among dapagliflozin patients.

Conclusion(s)

This study provides real-world evidence of head-to-head comparisons of dapagliflozin with a DPP-4 inhibitor. Our results suggest that while there was no difference in total healthcare costs overall between dapagliflozin and sitagliptin initiators, patients who initiated dapagliflozin as an add-on to OAD monotherapy had lower healthcare costs than sitagliptin initiators. Given the number of effective diabetes drugs currently on the market, this information may be of particular interest to patients, providers, and payers in their treatment decision-making.