Characteristics of and medication adherence for diabetic patients receiving dipeptidyl peptidase-4 inhibitors in US Medicare and commercial insurance plans

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Background

The dipeptidyl peptidase-4 (DPP-4) inhibitors are among the newer oral hypoglycemic diabetic medications which prevent the breakdown of incretin causing an increase in insulin release and a decrease in glucagon levels, thereby reducing blood glucose levels. This drug class is mainly indicated for management of type 2 diabetes as either monotherapy or in combination with other oral hypoglycemic agents. There are four DPP-4 inhibitors presently available in the US: sitagliptin marketed as Januvia, saxagliptin marketed as Onglyza, linagliptin marketed as Tradjenta, and alogliptin marketed as Nesina.

There is limited comparative evidence of these agents. A mixed treatment comparison meta-analysis of 83 randomized controlled trials reported similar efficacy and safety of DPP-4 inhibitors, with the exception of patients taking alogliptin plus metformin achieved HbA1c <7% more frequently than those treated with saxagliptin plus metformin [odds ratio 6.41 (95% CI 3.15-11.98) versus 2.17 (95% CI 1.56-2.95)].[1] A randomized, controlled, multi-country trial compared add-on therapy with saxagliptin or sitagliptin in patients whose glucose was inadequately controlled with metformin and found saxagliptin to be noninferior to sitagliptin.[2] The limited comparative evidence relied on data from clinical trials, which have limitations in generalizability to clinical practice. Thus, comparing medication adherence measured by prescription refill data can be informative since glycemic control improves with patient medication adherence.[3] A study conducted by Astra Zeneca reported significantly better adherence with saxagliptin compared to sitagliptin among a mixed population of commercial and Medicare beneficiaries.[4]

Objective

The objective of this study was to compare demographic characteristics, baseline clinical characteristics, adherence and persistence for patients taking DPP-4 inhibitors for both a Medicare cohort and a commercial plan cohort.

Methods

- Claims were extracted for Humana Medicare and commercial plan members with ≥1 prescription filled for a DPP-4 inhibitor between July 1, 2011 and March 31, 2013.
- The Medicare and commercial populations were analyzed separately.
- The first prescription claim for a DPP-4 inhibitor established the index date and index medication. Continuous enrollment was required 12-months pre-index and post-index date. Included patients were required to have had at least one refill of their index medication.
- Demographic characteristics were evaluated by age, gender, and geographic region between cohorts.
- The following clinical characteristics were evaluated:
  - Diabetes Complications Severity Index (DCSI): The DCSI quantifies the severity of the 7 diabetes complication categories and is used to asses patients' risk of adverse outcomes including hospitalizations and death.
  - Most recent pre-index HbA1c result (no more than 15 months prior to the index date) for the subset of patients with data available.
  - Costs were considered as a proxy for clinical severity. Mean pre-index health care costs (sum of plan and patient paid) were reported as total, pharmacy (Rx) and medical.
- Medication adherence was measured using the ratio of proportion of days covered (PDC) – i.e., days during the 12-month post-index period that the patient had an index medication available. Groups were compared using a generalized linear model, adjusting for DCSI, age, and gender.
- Persistence was determined using a 31-day gap in medication and compared between drug cohorts using Cox proportional hazard models.
- Alpha was set a priori at 0.05.

Results

Table 1. Sample Selection and Attrition

Few patients were prescribed alogliptin, and it was therefore not evaluated. Based on study criteria, 22,860 patients with Medicare coverage (17,292 sitagliptin; 4,282 saxagliptin and 1,286 linagliptin) and 3,229 patients with commercial coverage (2,368 sitagliptin; 643 saxagliptin and 218 linagliptin) were included.

Table 1a: Medicare Sample Selection and Attrition

Criteria	Patients Excluded n	Patients Excluded %	Patients Remaining n	Patients Remaining %
At least one prescription claim for a DPP-4 inhibitor during the identification period of July 1, 2011, to March 31, 2013			53,342	100%
12 months continuous enrollment before index DPP-4 inhibitor claim	23,216	43.5%	30,126	56.5%
12 months continuous enrollment after index DPP-4 inhibitor claim	2,794	5.2%	27,332	51.2%
At least one refill of index DPP-4 inhibitor	4,461	8.4%	22,871	42.9%
DPP-4 inhibitor was alogliptin (excluded)	11	0.0%	22,860	42.9%
Final Count			**22,860**	**42.9%**

Table 1b: Commercial Sample Selection and Attrition

Criteria	Patients Excluded n	Patients Excluded %	Patients Remaining n	Patients Remaining %
At least one prescription claim for a DPP-4 inhibitor during the identification period of July 1, 2011, to March 31, 2013			9,047	100%
12 months continuous enrollment before index DPP-4 inhibitor claim	4,167	7.8%	4,880	53.9%
12 months continuous enrollment after index DPP-4 inhibitor claim	1,057	2.0%	3,823	42.3%
At least one refill of index DPP-4 inhibitor	587	1.1%	3,236	35.8%
DPP-4 inhibitor was alogliptin (excluded)	7	0.0%	3,229	35.7%
Final Count			**3,229**	**35.7%**

Table 2. Demographic Characteristics

Demographic characteristics were similar between DPP-4 inhibitor cohorts, but Medicare patients were older and more likely to be female compared with commercial cohort (not tested statistically).

Table 2a. Medicare Baseline Demographics

Measure	Sitagliptin (n=17,292)	Saxagliptin (n=4,282)	Linagliptin (n=1,286)
Female, No. (%)	8,999 (52.0%)	2,180 (51.0%)	647 (50.3%)
Age, years, Mean (SD)	70.7 (±8.5)	70.2 (±8.5)	71.6 (±8.2)
Age Category, No. (%)			
<65	2,842 (16.4%)	760 (17.8%)	180 (14.0%)
65-69	4,285 (24.8%)	1,146 (26.8%)	276 (21.5%)
70-74	4,674 (27.0%)	1,112 (26.0%)	388 (30.2%)
75-79	3,018 (17.5%)	724 (16.9%)	235 (18.3%)
80+	2,473 (14.3%)	540 (12.6%)	207 (16.1%)
Geographic Region, No. (%)			
Northeast	401 (2.2%)	59 (1.3%)	22 (1.7%)
Midwest	3,769 (21.8%)	827 (19.3%)	214 (16.6%)
South	11,794 (68.2%)	3,064 (71.6%)	970 (75.4%)
West	1,328 (7.7%)	332 (7.8%)	80 (6.2%)

Table 2b. Commercial Baseline Demographics

Measure	Sitagliptin (n=2,368)	Saxagliptin (n=643)	Linagliptin (n=218)
Female, No. (%)	1,046 (44.2%)	282 (43.9%)	95 (44.0%)
Age, years, Mean (SD)	55.8 (±9.6)	55.5 (±9.7)	55.1 (±9.2)
Age Category, No. (%)			
<50	537 (22.7%)	165 (25.7%)	51 (23.4%)
50-54	440 (18.6%)	105 (16.3%)	47 (21.6%)
55-59	533 (22.5%)	146 (22.7%)	45 (20.6%)
60-64	540 (22.8%)	150 (23.3%)	51 (23.4%)
65+	318 (13.4%)	77 (12.0%)	24 (11.0%)
Geographic Region, No. (%)			
Northeast	4 (0.2%)	0 (0.0%)	0 (0.0%)
Midwest	714 (30.2%)	120 (18.7%)	33 (15.1%)
South	1,589 (67.1%)	511 (79.5%)	179 (82.1%)
West	61 (2.6%)	12 (1.9%)	6 (2.8%)

Table 3. Baseline Clinical Characteristics

Compared to other DPP-4 inhibitors, patients taking linagliptin had a higher DCSI score, used more insulin, and had higher pre-index costs in both the Medicare and commercial populations.

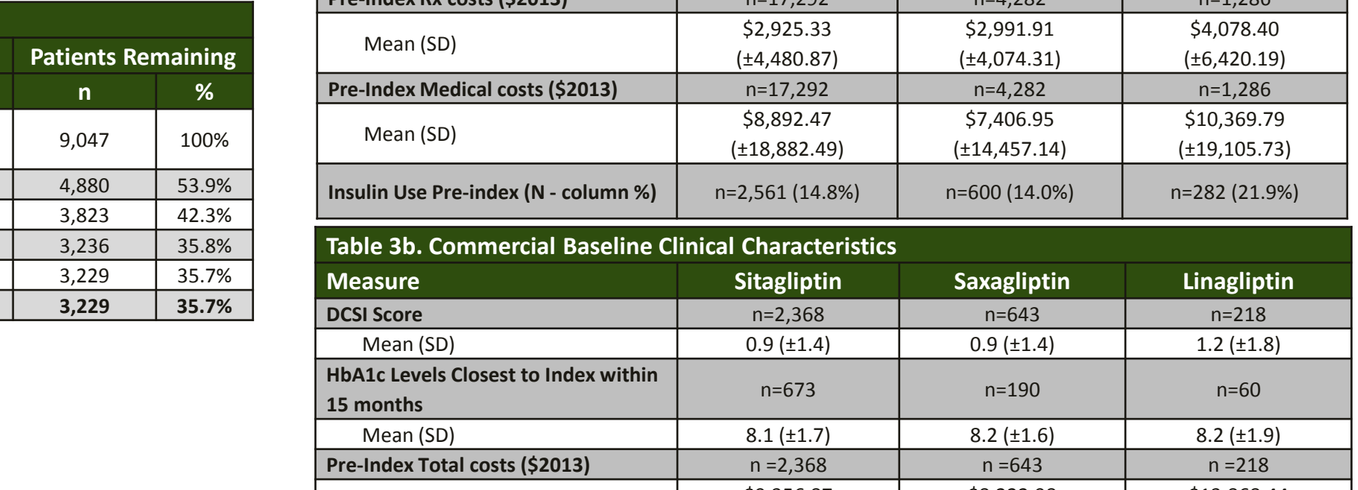
Table 3a. Medicare Baseline Clinical Characteristics

Measure	Sitagliptin	Saxagliptin	Linagliptin
DCSI Score	n=17,292	n=4,282	n=1,286
Mean (SD)	2.4 (±2.2)	2.2 (±2.0)	3.0 (±2.3)
HbA1c Levels Closest to Index within 15 months	n=6,616	n=1,583	n=507
Mean (SD)	7.8 (±1.5)	7.7 (±1.4)	7.7 (±1.4)
Pre-Index Total costs ($2013)	n=17,292	n=4,282	n=1,286
Mean (SD)	$11,817.80 (±19,974.99)	$10,398.86 (±15,659.18)	$14,448.19 (±20,800.48)
Pre-Index Rx costs ($2013)	n=17,292	n=4,282	n=1,286
Mean (SD)	$2,925.33 (±4,480.87)	$2,991.91 (±4,074.31)	$4,078.40 (±6,420.19)
Pre-Index Medical costs ($2013)	n=17,292	n=4,282	n=1,286
Mean (SD)	$8,892.47 (±18,882.49)	$7,406.95 (±14,457.14)	$10,369.79 (±19,105.73)
Insulin Use Pre-index (N - column %)	n=2,561 (14.8%)	n=600 (14.0%)	n=282 (21.9%)

Table 3b. Commercial Baseline Clinical Characteristics

Measure	Sitagliptin	Saxagliptin	Linagliptin
DCSI Score	n=2,368	n=643	n=218
Mean (SD)	0.9 (±1.4)	0.9 (±1.4)	1.2 (±1.8)
HbA1c Levels Closest to Index within 15 months	n=673	n=190	n=60
Mean (SD)	8.1 (±1.7)	8.2 (±1.6)	8.2 (±1.9)
Pre-Index Total costs ($2013)	n =2,368	n =643	n =218
Mean (SD)	$9,356.87 (±25,473.46)	$8,222.98 (±15,182.51)	$13,868.44 (±41,372.86)
Pre-Index Rx costs ($2013)	n=2,368	n=643	n=218
Mean (SD)	$2,576.02 (±4,350.78)	$2,940.83 (±6,162.05)	$4,060.37 (±7,941.48)
Pre-Index Medical costs ($2013)	n=2,368	n=643	n=218
Mean (SD)	$6,780.84 (±24,507.26)	$5,282.15 (±13,625.15)	$9,808.08 (±39,030.05)
Insulin Use Pre-index (N - column %)	n=253 (10.7%)	n=63 (9.8%)	n=39 (17.9%)

Figure 1. Adherence and Persistence



Adherence: Mean PDC was significantly lower in the linagliptin group vs. sitagliptin and saxagliptin in the Medicare population (p<0.0001). There were no between group differences in the commercial population.
Persistence: A higher proportion of the linagliptin group had gaps greater than 31 days vs. sitagliptin and saxagliptin in the Medicare population (P<0.0001). There were no between group differences in the commercial population.

Limitations

- Inherent biases in using claims data, including possibility of selection bias
- Medication refills do not mean that the patient consumed the medication
- HbA1c not available for all patients

Conclusions

- For both Medicare and commercial populations, baseline demographics were similar between the DPP-4 inhibitor medication groups, but patients on linagliptin may have been more complex (higher DCSI, more use of insulin at baseline).
- For the Medicare population, patients on linagliptin were less adherent and persistent than patients taking sitagliptin or saxagliptin, but differences may be due to complexity of linagliptin patients.
- In the commercial population, there were no differences in adherence or persistence between the drug groups.

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